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ON THE ACTION OF AQUEOUS SOLUTIONS OF ACIDS ON ALKENES

BY ARTHUR MICHAEL AND ROGER F. BRUNEL

[SECOND PAPER ON THE LAWS OF ADDITION IN ORGANIC CHEMISTRY[1]]

In examining the action of aqueous solutions of acids on alkenes we were led to question certain results obtained by Scheschukow[2] with regard to the action of aqueous hydriodic acid on isobutene. Scheschukow's statement was that if isobutene is passed through aqueous hydriodic acid saturated at 0° addition of the acid to the hydrocarbon with formation of tertiary butyl iodide takes place provided the acid has a greater concentration than that represented by $2HI + 11H_2O$ (1.7 specific gravity), but that at that concentration the reaction stops, i. e., isobutene ceases to take up hydriodic acid from the solution when the latter has the concentration of the stable hydrated acid.[3]

According to Roscoe[4] such a solution, at a pressure of 774 mm., contains 57 per cent. of hydriodic acid and distils unchanged at 127°; change of pressure alters the boiling point

[1] THIS JOURNAL, **41**, 118 (1909).

[2] Ber. d. chem. Ges., **19**, Ref. 544 (1886). Bull. soc. chim., [2] **42**, 329; **46**, 823. The original paper (J. Russ. Phys. Chem Soc., **1886**, I, 204) is not accessible to us.

[3] Bineau: Ann. chim. phys., [3] **7**, 266.

[4] Ann. Chem. (Liebig), **116**, 203 (1860).

and consequently the composition of the distillate, but the effect is not great. Roscoe and Dittmar[1] showed that the liquid obtained by distillation at any temperature has the same composition as that obtained by passing air or hydrogen for some time through the solution at the same temperature. Roscoe thought the change in composition with pressure sufficient evidence against the existence of such solutions as definite compounds, but with compounds of such an unstable nature this conclusion does not necessarily follow. However, a consideration of the vapor pressure diagram[2] shows that the particular composition of the highest boiling solution, being that at which the mixture of vapors has the same composition as the residual solution, is merely a matter of chance. Such a solution of highest boiling point or minimum vapor pressure will exist in general when the vapor of each constituent is readily soluble in the other constituent. This great solubility is doubtless an indication of affinity between such constituents and of a tendency to form more or less definite compounds, but the composition of the highest boiling solution has no evident connection with that of any compound that may exist in the solution. Scheschukow's statements, if correct, would raise doubt as to the soundness of the above reasoning, since they seemed to give evidence of the existence of a compound of the composition $2HI.11H_2O$, but on repeating his experiments we find that his observations are not correct.

If isobutene is passed through aqueous hydriodic acid saturated at 0°, absorption is at first quite rapid and a layer of tertiary butyl iodide is soon formed. After a time the rate of absorption decreases and, if the experiment is stopped when the iodide is very slowly formed, an acid of about the specific gravity 1.7 is obtained. The addition, however, by no means ceases at that point, as will be seen from the following experiments.

Isobutene was passed through hydriodic acid of specific gravity 1.9, cooled in ice, and when the gas appeared to pass through unabsorbed the experiment was stopped. The solu-

[1] Ann. Chem. (Liebig), **112**, 347 (1859).
[2] Nernst: Theoret. Chem. (6te Auflage), 110.

tion was slightly turbid and was allowed to stand until it became clear. The specific gravity of the acid layer was found to be 1.664. With hydriodic acid of specific gravity 1.90 at 17°, when the rapid absorption was over the gravity of the acid solutions in three experiments was found to be 1.642, 1.678, and 1.675.[1] The above solution of specific gravity 1.678, on further passage of isobutene, slowly gave a layer of iodide. In another experiment an acid of gravity 1.623 was used, and after 1.3 liters of isobutene were passed through it in two hours, the gravity had diminished to 1.588; a layer of iodide had formed and the acid solution contained some tertiary butylcarbinol. Similar results were obtained with freshly prepared solutions of hydriodic acid having the specific gravities 1.63 and 1.618. It is evident that although the velocity of solution decreases considerably when the concentration of about 60 per cent. hydriodic acid is reached, absorption does not cease; moreover, the rate of formation of a layer of the butyl iodide is no longer a criterion for the rate of absorption of the gas, as at that point part of the hydrocarbon dissolves, with formation of the soluble, tertiary carbinol.

We then made similar experiments with trimethylethylene and hydrobromic acid. These were carried out in small sealed tubes, which were shaken, in some cases for only a few hours, but usually for some days or even weeks. When carbinol alone was formed the end of the reaction could be recognized by complete solution of the hydrocarbon; when bromide was formed the reaction could be followed by titration of the acid remaining. Only 1–3 cc. of acid were used in each experiment, the measurements being made with a 1 cc. burette graduated to 0.01 cc. When the amylene formed partly bromide and partly carbinol the amount of bromide was determined by titration of the residual acid and the rest was assumed to have formed carbinol, there being no other obvious possibility.

In the following table, Column 2 gives the ratio in mole-

[1] According to Roscoe the solution of minimum vapor pressure at 17° has a composition of 60.5 per cent., or a specific gravity a little over 1.71.

cules of water to hydrobromic acid in the solution used, and Column 6 the same ratio after the reaction. Column 5 shows what percentage of the hydrocarbon was converted into bromide. An excess of acid was used, as shown in Column 3, in order to avoid a decided change in concentration during the reaction. In experiments where two times are given[1] they refer to two experiments with the concentration concerned:

Table I

Normality of acid	H_2O : HBr Mols.	HBr : C_5H_{10} Mols.	Time Hours	Time Hours	Bromide Per cent.[2]	H_2O : HBr in resid. sol.
9.66	4.4	5.0	10	24	91–92	5.4
8.06	5.47	4.0	40	64	76	6.7
7.64	5.99	5.0	40	72	69	6.9
6.98	6.5	5.0	16	90	67	7.5
5.54	8.51	4.4	3	3	2	8.3
4.56	10.8	6.0	4		0	10.6

It will be noted that a 9.66 N acid forms largely bromide; one more dilute than 5.54 N only carbinol;[3] intermediate concentrations, mixtures of the two compounds. From the concentrations of the residual acids we may conclude that a solution of about $8H_2O$: 1HBr would form carbinol and bromide in the ratio in which the water and acid are present.

With regard to the mechanism of the reaction there are three possibilities, disregarding the question of ionization. First, the carbinol may in all cases be formed first and then react with the acid to a greater or less extent, forming bromide; secondly, the acid may always add directly, so that the bromide is the intermediate product; and, lastly, both the water and acid may act simultaneously. We have no conclusive evidence for either view, but the following facts have some bearing on the question.

[1] The times given in the table do not indicate the time required for the reaction to reach an end, but are given merely to show that times far enough apart were chosen to prove that the reaction had reached completion. Apparently, however, the rate of solution or reaction of the hydrocarbon decreases steadily from the most to the least concentrated solution.

[2] As will be seen from the experimental details below, the result given in the table is the means of results agreeing within the limits of accuracy of the method used.

[3] These are not the minimum and maximum concentrations, respectively, at which these results would be obtained, but are merely those of solutions made up arbitrarily beforehand which gave these results.

That the carbinol should always be the intermediate product seems very improbable when all the facts are considered. Tertiary amyl alcohol reacts with aqueous hydrobromic acid almost instantaneously, giving the corresponding bromide, provided the concentration of the acid is great enough so that it will react at all. If the amylene is converted into bromide by aqueous acids through the two steps amylene $\longrightarrow$ carbinol $\longrightarrow$ bromide, it must, therefore, be the first stage of the reaction that determines its velocity. The hydrocarbon, like the other alkenes, does not dissolve at all in pure water, so that the acid is evidently necessary as a catalytic agent. A very slight amount of acid is sufficient to cause the solution to take place slowly, and the rate increases, as would be expected, with the concentration of the catalyzing acid. The fact that is hard to explain, however, is that the velocity of solution—or reaction—continues up to the point where the concentration of acid is so great that there is very little water present. The reaction with pure, i. e., gaseous, hydrobromic acid is of course not comparable with that where the aqueous solutions are concerned; but if we use solutions of sulphuric acid we find that the rate of reaction increases with the concentration of the acid right up to acid of nearly 100 per cent. It would have to be a very marked catalytic effect on the part of the acid that would bring about a reaction of such great velocity when the concentration of the water becomes so small.

With regard to the second possibility, i. e., the intermediate formation of bromide, that also is possible as far as the reactivity of the bromide with water is concerned. Michael and Leupold[1] have shown that if tertiary amyl bromide is shaken with water it is dissolved in a half hour. In the solutions where the amylene dissolves, giving carbinol with greatest rapidity (4.56–5.54 N), the time required is several hours, which is thus long enough for the bromide, if formed, to be decomposed. It is to be noted, however, that all acids appear to catalyze the formation of tertiary alcohol from the amylene, whereas some of them are incapable of forming addition products with the hydrocarbon, such, for, example, as ben-

[1] Ann. Chem. (Liebig), **379**, 290 (1911).

zenesulphonic acid (see below). Here the reaction would appear to be directly with the water.

It seems probable, therefore, that the hydrocarbon reacts with both the water and acid simultaneously. But the familiar test for such side reactions, i. e., the examination of the ratio of the products at intervals as the reaction progresses to see if it is constant, cannot be applied here, since the products, the carbinol and the bromide, are convertible into each other with a velocity at least as great as that of their formation from the amylene, so that the examination of these products gives us data only for the esterification equilibrium between them and the acid and water.

As seen in Table I, with an acid of a strength somewhere between $HBr + 6.5H_2O$ and $HBr + 8.5H_2O$, there would be no change in the ratio of acid to water during the addition. The high heat of solution of hydrobromic acid in water indicates the formation of compounds,[1] and it may be that some such product with the composition of about $HBr : 8H_2O$ represents the most stable system that these substances are capable of forming, for it is very improbable that such products are altogether definite in composition. When a considerable excess of water or acid is present, it then reacts more readily than either of them, when they are in the proportion of the comparatively stable product or system. At that particular point the alkene should act with amounts of water and acid in the same ratio, which would be the case, as pointed out above, with an acid of about the composition $HBr : 8H_2O$. This concentration is quite different from that of a constant boiling acid, which is $HBr : 5H_2O$.

An explanation of these relations may perhaps be found in the assumption that the formation of halide or carbinol from amylene proceeds with union of the acid + water to a binary "polymolecule," which, with the hydrocarbon, forms a larger ternary "polymolecule."[2] Since there is an accumulation

[1] See Pickering: Phil. Mag., [5] **36**, 111 (1893).

[2] Michael and Leupold (Ann. Chem. Liebig, **388**, 257) have shown that tertiary amyl alcohol unites with water and strong mineral acids to form "polymolecules," which at about 75° decompose with separation of amylene. On shaking this mixture at ordinary temperature the amylene dissolves with formation of tertiary carbinol. These relations accord with the view that the carbinol is formed by the direct union of the hydrocarbon with water, the acid acting catalytically.

of free *chemical* energy in the formation of the ternary "polymolecule" it is able to do work that cannot be done by free amylene alone, which explains why acids, as well as water, act catalytically in these addition reactions. Further, since the solution of hydrobromic acid in water is exothermic, to effect the second stage of the reaction, that is, the breaking down of the ternary "polymolecule" into halide or carbinol and acid + water, a chemical hindrance has to be overcome which is the separation of a molecule of either acid or water from the binary part of the "polymolecule." If the acid is present in a much greater proportion than water, it should be easier to eliminate a molecule of it than one of water, and, reversely, if water is present in large excess, a molecule of that compound should be easier to remove than one of acid. From this point of view, the decomposition of x "polymolecules" of $C_5H_{10}.HBr.8H_2O$, proceeds with the formation of $x/2$ molecules of halide and of carbinol, and any system containing acid in a greater or less relation should lead to the formation of halide in a greater or less proportion.

The combination of water with alkenes resembles the hydrolysis of methyl acetate and of sugar, and it seemed of interest to ascertain whether the catalytic effects of acids stand in the same relation to each other in the first as they do in the latter reactions. For this purpose, the velocity of solution of trimethylethylene and isobutene in dilute solutions of acids was examined. Solutions of hydriodic acid (2.045 N), of hydrobromic acid (2.065 N) and of hydrochloric acid (2.058 N) were prepared, whose concentration of hydrogen ions were approximately the same. Two cc. of each solution were sealed in a small tube with 0.06 cc. of amylene and the tubes shaken at the same time until solution was effected. This took place in 140 minutes with hydriodic acid, in 200 with hydrobromic acid, and in 300 with hydrochloric acid. In a second series, the temperature was somewhat different and the times were longer, 280, 480 and 700 minutes, respectively, but these results stand approximately in the same relation to each other as those obtained in the preceding series. Solutions were then prepared, which, in accordance with

known conductivity data, should have been isohydric. According to the titrations, they varied less than 1 per cent. from the calculated values. The results are as follows: with hydriodic acid (2.576 N) solution of the amylene took place in 18 days; with hydrochloric acid (2.525 N) in 23 days; and with trichloroacetic acid (2.052 N) it was still incomplete after 40 days. In another series of experiments the following results were obtained: with hydriodic acid (2.509 N) 12 days; benzenesulphonic acid (2.420 N) came next and effected solution very little before hydrobromic acid (2.550 N), which required 13 days; and with trichloroacetic acid (2.063 N), a considerable part of the hydrocarbon was undissolved in that time. Solutions of sulphuric, oxalic and phosphoric acids were next made, which contained acid and water in the proportion of one to eighty and whose molecular normalities were 0.687, 0.673 and 0.677. Two cc. of acid were placed in a tube, the weight taken, liquid isobutylene added, the tube closed and again weighed. The sulphuric acid tubes contained 0.139 and 0.138 gram of isobutylene and solution took place in 7 days. The oxalic acid tubes with 0.131 and 0.134 gram hydrocarbon took 33 and 34 days; the phosphoric acid tube contained 0.139 gram isobutylene and was broken after 35 days, but only about one-half had dissolved in that time.

It will be observed that there is a rough agreement with the relations found by the hydrolysis methods, and therefore also with the ionization constants of the acids. The order of reactivity with strong mineral acids stands, however, in a closer relationship to that found by sugar inversion than it does to that found by ester hydrolysis, or to that found by conductivity. Thus, according to the latter method, the relation of the constants of hydrochloric to hydrobromic acid is 100 : 100.1; with the methyl acetate method it is 100 : 98; while with the sugar inversion method it is 100 : 111. By the last method is obtained a decidedly higher value for hydrobromic than for hydrochloric acid, which relation also obtains in the addition of water to amylene. With benzenesulphonic acid the catalytic influence in causing water addition to amylene stands slightly higher than that of hydrochloric acid, which is

also the case in sugar inversion (104 to 100), while in the ester hydrolysis the values are nearly the same (99 to 100), and the conductivity method shows a decidedly lower value (74.8 to 100).

It is remarkable that the order in which hydriodic, hydrobromic and hydrochloric acids, in dilute solution, exert a catalytic influence in inducing the addition of water to amylene is the same as that of the facility of addition of the acids themselves to unsaturated hydrocarbons, and also that of the reactivity of these acids in converting carbinols into halides.[1] This relation could be explained by assuming that the formation of carbinol from alkene is not direct, but passes through that of the iodide, bromide and chloride, since the ease of conversion of these different alkyl halides by water into carbinol proceeds in the same order.

As shown above, there is an objection to this assumption in the inability of benzenesulphonic acid to form addition products with the alkenes.

If, as seems probable, the elimination of water from the "polymolecules" may be effected more easily when hydriodic acid is present than when hydrobromic acid, and still less easily when hydrochloric acid is present, the above relations in the addition of water to the hydrocarbons would be explained.

EXPERIMENTAL PART

For the repetition of Scheschukow's experiments, hydriodic acid from Kahlbaum, of specific gravity 1.90, was used. The specific gravities were determined in a 3 cc. pycnometer of the Sprengel type with thermometer fused in, easily capable of accuracy to less than 0.1 per cent. About 5 cc. of acid were used for each experiment. This was placed in a test tube and the gas passed in through a tube drawn out to a fine point. As the tertiary iodide is decomposed by aqueous hydriodic acid when the concentration is below about 1.7 specific gravity, the layer of iodide formed was separated, when it no longer increased fast, as completely as possible by a pipette. In some cases it was separated several times as the reaction progressed.

[1] These relations do not agree with the assumption that the reactions in question proceed through ionization. The ease of addition appears to be determined by the chemical hindrance, i. e., the energy required to separate the halogen from hydrogen.

Trimethylethylene with Aqueous Hydrobromic Acid Solutions

The hydrobromic acid solutions for the following experiments were standardized by titration from a 1 cc. burette graduated to 0.01 cc. against potassium hydroxide from a 50 cc. burette, with methyl orange as indicator. In all experiments given below the alkali, unless otherwise stated, was 0.591 N. One gram of amylene is equivalent to 24.14 cc. of this solution. The ratio of water to acid is expressed in numbers of molecules; the per cent. of acid by weight. The tubes were filled, sealed and shaken vigorously for the time indicated. After the first few experiments, in case there was a layer of bromide formed on top of the acid solution, the latter (lower layer) was removed by a pipette and titrated; the oil was then shaken out with a little water, which was removed and added to the titrated solution and alkali again added to an end point. This was repeated until the titration of the wash water was either zero or constant for successive washings. As the tertiary amyl bromide is slowly decomposed on shaking with water, the titration of this wash water was not zero if the shaking with the oil was prolonged. Only the final end points are given below, but it is indicated whether or not such a washing process was carried out. The difference between the alkali used for titration and that which would neutralize all the acid used is equivalent to the amyl bromide formed. The difference between this amount of alkali and that which would correspond to all the amylene taken is equivalent to the amylene converted into carbinol.

HBr 9.66 N. 4.4H_2O : 1HBr (50.8 Per cent. HBr).—Two tubes were prepared each containing 0.210 gram amylene and 1.555 cc. acid (= 25.41 cc. KOH), i. e., 5 molecules of acid:

Time	I 10 hrs. (oil not washed)	II 24 hrs. (oil not washed)
KOH to titrate	20.72	20.80
KOH = bromide formed	4.69	4.61
KOH = amylene taken	5.08	5.08
KOH = carbinol formed	0.39	0.47
Per cent. bromide	92.0	91.0

Residual acid (mean) 5.17H_2O : 1HBr

HBr 8.06 N. 5.47H_2O : 1HBr (45.1 Per cent. HBr).—Two tubes were prepared, each containing 0.225 gram amylene and 1.600 cc. acid (= 21.82 cc. KOH), i. e., about 4 molecules of acid.

	I	II
Time	40 hrs. (oil not washed)	64 hrs. (oil washed)
KOH to titrate	17.60	17.73
KOH = bromide formed	4.22	4.09
KOH = amylene taken	5.43	5.43
KOH = carbinol formed	1.21	1.34
Per cent. bromide	77.7	75.3

Residual acid (mean) 6.7H_2O : HBr

HBr 7.64 N. 5.99H_2O : 1HBr (42.9 Per cent. HBr).—Two tubes each with 0.200 gram amylene, 1.890 cc. acid (= 24.30 cc. KOH), i. e., 5 molecules of acid.

	I	II
Time	72 hrs. (oil washed)	40 hrs. (oil washed)
KOH to titrate	21.02	21.02
KOH = bromide formed	3.28	
KOH = amylene taken	4.82	Same as I
KOH = carbinol formed	1.54	
Per cent. bromide	68.1	

Residual acid, 6.9H_2O : 1HBr

HBr 6.98 N. 6.5H_2O : 1HBr (40.8 Per cent. HBr).—Two tubes, each with 0.200 gram amylene, 2.000 cc. acid (= 23.62 cc. KOH), i. e., 4.9 molecules HBr.

	I	II
Time	16 hrs. (oil not washed)	90 hrs. (oil washed)
KOH to titrate	20.45	20.32
KOH = bromide formed	3.17	3.30
KOH = amylene taken	4.82	4.82
KOH = carbinol formed	1.65	1.52
Per cent. bromide	65.8	68.6

Residual acid (mean), 7.48H_2O : 1HBr

HBr 5.54 N. 8.51H_2O : 1HBr (34.3 Per cent. HBr).—Two tubes were prepared, each with 0.200 gram amylene and 2.000 cc. acid (= 18.74 cc. KOH), i. e., 3.9 molecules HBr. A homogeneous solution was formed in less than 3 hours.

	I	II
Time	20 hrs.	3 hrs.
KOH to titrate	18.67	18.60
KOH = bromide formed	0.07	0.14
KOH = amylene taken	4.83	4.83
KOH = carbinol formed	4.76	4.69
Per cent. bromide	1.4	3.0

Residual acid (mean), $8.3H_2O$: 1HBr

HBr 4.56 N. 10.8H_2O : 1HBr (29.5 Per cent. HBr).—One tube with 0.100 gram amylene, 1.886 cc. acid (= 99.43 cc. 0.0865 N KOH), i. e., 6 mols. HBr.

	I
Time	4 hrs.
KOH to titrate	99.62
KOH = bromide formed	0.00
KOH = amylene taken	16.57
Per cent. bromide	0.0

Residual acid, $10.6H_2O$: 1HBr

In all cases above where much carbinol was formed, the solution, after titration, was distilled and the carbinol salted out from the first portion of the distillate by potash. In all experiments also the oil was distilled. The boiling point, where the amount was sufficient to give it with fair accuracy, was always from some point not below 95° or 100° to about 105°–108°. The boiling point of the tertiary alcohol is 101°–102°; that of the bromide 108°–109°.

Several experiments were carried out with tetramethylene and diisobutylene, but in all cases but one it was found that unchanged hydrocarbon was present, by the fact that complete solution in no case occurred.

HBr 8.06 N. 5.47H_2O : 1H_2O (45.1 Per cent. HBr).—Two tubes were prepared, each with 0.270 gram tetramethylethylene, 1.601 cc. acid (= 25.20 cc. KOH 0.5115 N), i. e., 4 molecules acid.

	I	II
Time	53 days (oil washed)	85 days
KOH to titrate	20.20	20.35
KOH = bromide formed	5.01	4.86
KOH = hexene used	6.28	6.28
KOH = carbinol formed	1.27	1.42
Per cent. bromide	80.0	77.4

Boiling Point of Oil.—About half distilled at near 120°, the rest went up to 130° or 135°. First lot redistilled and boiled at about 115°. Boiling point of the hexene, 72°; of tertiary hexylcarbinol, 117°; of bromide, about 135°–140°.

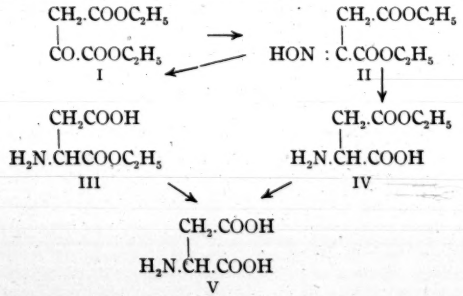
[Contributions from the Sheffield Laboratory of Yale University]

CCII —RESEARCHES ON PYRIMIDINES
THE ACTION OF HYDROXYLAMINE ON 4-METHYL-6-OXYPYRIMIDINE-2-OXALOTHIOGLYCOLLIC ACID. β-MERCAPTO-α-OXIMIDO-PROPIONIC ACID

By Treat B. Johnson and Norman A. Shepard

[FIFTY-SIXTH PAPER]

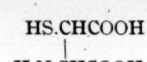
Piutti[1] synthesized aspartic acid from diethyl oxaloacetate in the following manner: The diethyl ester (I) was first converted into its oxime (II) and the latter then reduced, in an aqueous solution, with sodium amalgam. A mixture of the two isomeric esters, α-ethyl aspartate (III) and β-ethyl aspartate (IV), was obtained, which gave, by saponification, the inactive aspartic acid (V). This synthesis is represented by the following structural formulas:



The chief aim of the work described in this paper was to investigate the action of hydroxylamine on a mercapto deriva-

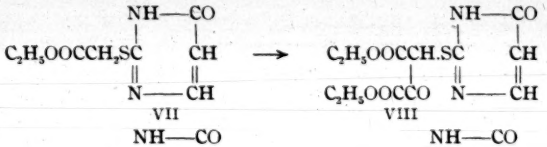
[1] Atti accad. Lincei, **1887**, 300. Gazz. chim. ital., **18**, 457. Ber. d. chem. Ges., **21**, Ref., 351. *Ibid.*, **22**, Ref., 241.

tive of diethyl oxaloacetate with the possibility of developing a synthesis of the unknown amino acid, *aminomercaptosuccinic acid* (VI).

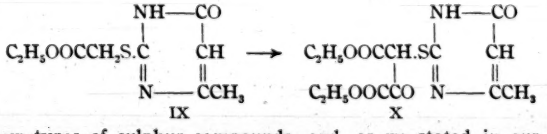


VI

In a previous paper from this laboratory[1] the writers have shown that diethyl oxalate condenses with certain pyrimidinethioglycollates, in alcohol solution and in the presence of sodium ethylate, forming the corresponding pyrimidineoxalothioglycollates. For example, ethyl 6-oxypyrimidine-2-thioglycollate (VII) and ethyl 4-methyl-6-oxypyrimidine-2-thioglycollate (IX) condensed with diethyl oxalate, forming diethyl 6-oxypyrimidine-2-oxalothioglycollate (VIII) and diethyl 4-methyl-6-oxypyrimidine-2-oxalothioglycollate (X), respectively. These β-ketone esters (VIII) and (X) represent



VII VIII



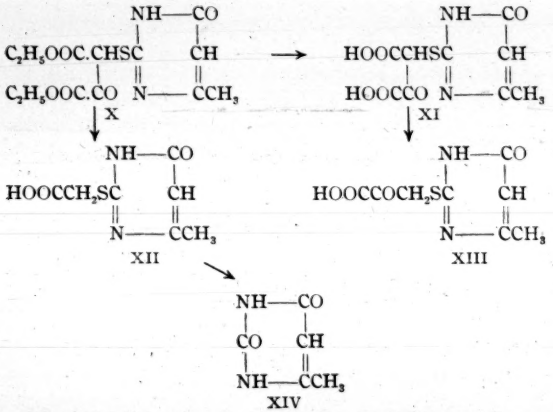
IX X

new types of sulphur compounds, and, as we stated in our previous paper,[2] are of interest because of their possible use for further syntheses. The ester (X) is the foundation of this research and was selected for our work because it is a crystalline compound and can be prepared easily in large quantities.

Diethyl 4-methyl-6-oxypyrimidine-2-oxalothioglycollate (X) undergoes smoothly the acid and ketone hydrolyses typical of β-ketone esters. When warmed with alkali it undergoes

[1] THIS JOURNAL, **48**, 346.
[2] *Loc. cit.*

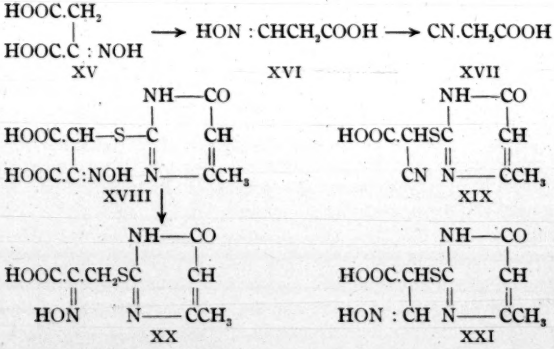
saponification, oxalic acid is detached and 4-methyl-6-oxypyrimidine-2-thioglycollic acid (XII) is formed. On the other hand, when digested with hydrochloric acid, ethyl chloride is evolved and the dibasic acid (XI) is produced. This acid, however, is unstable and loses carbon dioxide on long digestion and is transformed quantitatively into the pyruvic acid derivative, 4-methyl-6-oxypyrimidine-2-thiopyruvic acid (XIII). It is a remarkable fact that this acid (XIII) is so stable in the presence of boiling hydrochloric acid while the corresponding 2-thioglycollic acid (XII) is transformed quantitatively, under the same conditions, into thioglycollic acid and methyluracil (XIV):



We have investigated the action of hydroxylamine on 4-methyl-6-oxypyrimidine-2-oxalothioglycollic acid (XI), its diethyl ester (X) and also 4-methyl-6-oxypyrimidine-2-thiopyruvic acid (XIII). We find that the dibasic acid (XI) reacts with hydroxylamine, giving three definite compounds. The primary product of the reaction is apparently the oxime (XVIII) corresponding to oximidosuccinic acid (XV), which has been described by Hantzsch and Cramer.[1] This oxime,

[1] Ber. d. chem. Ges., **24**, 1192, 1198.

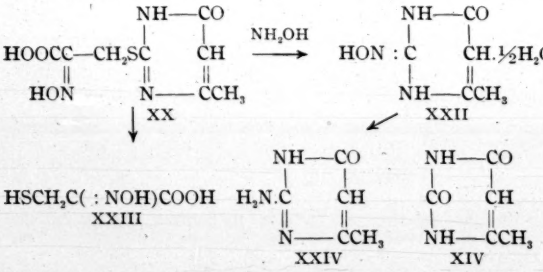
however, was not isolated. It was unstable and lost a molecule of carbon dioxide, at ordinary temperature, forming the oxime of 4-methyl-6-oxypyrimidine-2-thiopyruvic acid (XX). This manner of decomposition is unique, since the prototype of this series of acids, oximidosuccinic acid (XV), which occurs in two stereoisomeric modifications, breaks down in an entirely different way with formation of water, carbon dioxide and cyanoacetic acid (XVII).[1] We obtained no evidence of the formation of any 4-methyl-6-oxypyrimidine-2-cyanoacetic acid (XIX) or the oximido acid (XXI). In other words, it is the carboxyl group in the β-position with respect to the oxime group which is detached in the pyrimidine derivative (XVIII), while it is the α-carboxyl which is detached in the case of Cramer's oximidosuccinic acid (XV). Cramer[2] writes as follows: "Dieser Zerfall der β-Oximidobernsteinsäure vollzieht sich aber merkwürdigerweise bereits bei gewöhnlicher Temperatur und bei der vollständig trockenen Substanz. Die frisch bereitete Säure nimmt beim Stehen im Exsiccator über Kali anfangs rasch, schliesslich langsam an Gewicht, ab; doch konnte die Zersetzung nicht bis zu Ende verfolgt werden, da die Substanz mit Eisenchlorid sich immer noch blau färbte, also noch unveränderte β-Oximidobernsteinsäure enthielt."



[1] Hantzsch and Cramer: *Loc. cit.*
[2] Ber. d. chem. Ges., **24**, 1207.

This difference in the behavior of these two acids is truly remarkable. These interesting changes are represented by the above formulas.

That we were dealing with the α-oximido acid (XX) and not with a β-derivative (XXI) corresponding to the β-oximidopropionic acid (XVI)[1] was established by the following facts: We stated above that the oxalothioglycollic acid (XI) reacts with hydroxylamine to form not only the oxime (XX) but also two other derivatives. We find that the pyruvic acid (XIII) reacts with hydroxylamine and forms the same substances as are obtained from the oxalothioglycollic acid (XI). While the oxime (XX) could be isolated and purified, on the other hand it is unstable in the presence of free hydroxylamine. Under these conditions, the bond between the sulphur and carbon in the pyrimidine nucleus is ruptured and β-mercapto-α-oximidopropionic acid (XXIII) and 2-oximido-4-methyl-6-oxypyrimidine (XXII) are formed quantitatively. These derivatives are of interest as they are representatives of two new types of organic compounds. The formation of the same substances from the pyruvic acid (XIII) and the oxalothioglycollic acid (XI) is proof, therefore, that the oxime (XVIII) loses that carboxyl group which is joined to the —CHS— grouping. An attempt to reduce the oximidopyrimidine (XXII) to 2-amino-4-methyl-6-oxypyrimidine (XXIV) with stannous chloride in hydrochloric acid solution was unsuccessful. The oxime underwent hydrolysis and methyluracil (XIV) was formed.

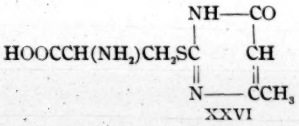


[1] Pechmann: Ann. Chem. (Liebig), **264**, 286. Hantzsch: Ber. d. chem. Ges. **25**, 1904.

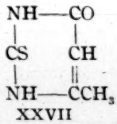
We have now investigated the behavior, towards reducing agents, of the two oximes, β-mercapto-α-oximidopropionic acid (XXIII) and its pyrimidine derivative (XX). We have reduced these two acids in alkaline, acid and neutral solutions, but in no case did we succeed in obtaining cysteine (XXV), or the pyrimidine derivative of this amino acid (XXVI). On the other hand, both acids are unstable and undergo com-

$$HS.CH_2.CH.(NH_2).COOH$$

XXV



XXVI



XXVII

plete decomposition with reduction of the β-mercapto groupings and the α-oximido groups with formation of alanine. The sulphur was obtained in the form of hydrogen sulphide and 2-thio-4-methyluracil (XXVII), respectively. While we obtained conclusive evidence of the formation of alanine, the yield of this acid, however, was extremely small. This is explained by the fact that the greater portion of the oximido acids undergoes hydrolysis, before reduction, with formation of hydroxylamine, which is then reduced to ammonia. The reduction of the oximido acid (XX) is expressed by the following equation:

$$HOOCC(:NOH)CH_2S.(C_5H_5ON_2) + 3H_2 = CH_3CH(NH_2)COOH + H_2O + C_5H_5ON_2S$$

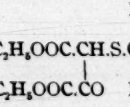
The investigation of oximes containing the grouping

$$HON:\overset{|}{C}—\overset{|}{CH}—S—$$

will be continued.

EXPERIMENTAL PART

Diethyl 4-Methyl-6-oxypyrimidine-2-oxalothioglycollate,



.—This pyrimidine has been de-

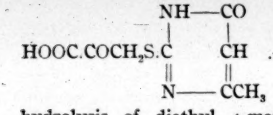
scribed in a previous paper from this laboratory.[1] Since it was the starting point for our investigation we have had occasion to prepare it several times and consequently will give here the best conditions for preparing it in large quantities. One molecular proportion of ethyl 4-methyl-6-oxypyrimidine-2-thioglycollate[1] is dissolved in 5 parts of absolute alcohol containing 2.25–2.5 atoms of sodium in the form of sodium ethylate. One and one-half molecular proportions of diethyl oxalate are then added to the cool solution and the mixture allowed to stand, protected from the air, at ordinary temperature. Working with 10 grams of thioglycollate at a time, it has been our experience that the condensation is complete in about 20 hours. In most cases, however, we allowed the reaction to proceed for a much longer time. In one experiment, for example, from 30.0 grams of the glycollate we obtained 34.0 grams of the pure condensation product, corresponding to 80.0 per cent. of the theoretical yield. After the condensation was complete an excess of ether was then added to the mixture, when the yellow sodium salt of the ketone ester deposited in a granular condition. This salt is very hygroscopic and dissolves immediately in cold water. The pyrimidine was obtained by addition of acetic acid, in slight excess, to this aqueous solution of its sodium salt. It deposited in colorless prisms, which melted without further purification at 138°–139°. A mixture of this substance with the original thioglycollate melted at 125°–130°. It was purified by recrystallization from alcohol and melted at 140°. It separated from alcohol in characteristic, hexagonal tables or prisms. The results of six of our experiments are recorded in the following table:

Table I

	$C_2H_5O_2CCH_2SC(N{=}CCH_3)CH{=}CNH{-}CO$ Grams	$COOC_2H_5$ $COOC_2H_5$ Grams	Sodium Grams	Time	Yield of pyrimidine Grams	Per cent. of theory
1	20.0	19.2	4.0	6 days	22.5	78.4
2	40.0	38.4	8.0	12 days	36.0	62.7
3	40.0	38.4	8.0	15 days	40.0	70.0
4	10.0	9.6	2.5	20 hours	10.7	74.8
5	10.0	9.6	2.5	20 hours	10.7	74.8
6	30.0	28.8	6.75	5–6 days	34.0	80.0

[1] Johnson and Shepard: *Loc. cit.*

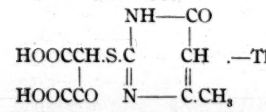
4-Methyl-6-oxypyrimidine-2-thiopyruvic Acid,



.—This acid is easily prepared by hydrolysis of diethyl 4-methyl-6-oxypyrimidine-2-oxalothioglycollate with hydrochloric acid. Ten grams of the ester were dissolved in 20–30 cc. of concentrated hydrochloric acid and the solution evaporated to dryness on the steam bath. This operation was repeated twice, in each case with 20 cc. of hydrochloric acid. This pyruvic acid was thus obtained in a crystalline condition and melted without further purification at 180°–185°. It is soluble in hot water and difficultly soluble in boiling alcohol. It was purified, for analysis, by recrystallization from water and separated, on cooling, in hexagonal prisms, which melted at 210°–212° with effervescence. The yield was good. Analysis (Kjeldahl):

	Calculated for $C_7H_8O_4N_2S$	Found	
		I	II
N	12.28	12.16	12.34

4-Methyl-6-oxypyrimidine-2-oxalothioglycollic Acid,



.—This dibasic acid can be obtained easily by careful hydrolysis of diethyl 4-methyl-6-oxypyrimidine-2-oxalothioglycollate. Twenty-two and four-tenths grams of this ester were suspended in 80 cc. of concentrated hydrochloric acid in an evaporating dish. On warming, it completely dissolved and ethyl chloride was evolved. The solution was then evaporated almost to dryness when the acid was obtained as a syrup, which immediately solidified on cooling. The crude acid melted at 150°–160°. It is extremely soluble in cold water and boiling alcohol, and insoluble in chloroform. It crystallizes from alcohol in rosettes of slender prisms, which melt at 159°–161° with evolution of carbon

dioxide. The yield of purified material was generally from 70–80 per cent. of the theoretical. Analysis (Kjeldahl):

	Calculated for $C_9H_8O_3N_2S$	Found I	Found II
N	10.29	10.28	10.20

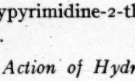
Action of Potassium Hydroxide on Diethyl 4-Methyl-6-oxypyrimidine-2-oxalothioglycollate

Four-tenths of a gram of potassium hydroxide was dissolved in 15–20 cc. of water and 2.0 grams of this pyrimidine dissolved in the solution. The mixture was then heated on the steam bath for one hour and finally cooled. Ethyl 4-methyl-6-oxypyrimidine-2-thioglycollate separated and melted at 145°-146°.

The Action of Hydroxylamine on 4-Methyl-6-oxypyrimidine-2-oxalothioglycollic Acid

Experiment 1

2-Oximido-4-methyl-6-oxypyrimidine,



$HON:C_4H_2N_2(CH_3)(O) \cdot \frac{1}{2}H_2O$.—Two and two-tenths grams of sodium hydroxide (3 mols.) were dissolved in 5 cc. of water and 5 grams of the oxalothioglycollate acid dissolved in the cold solution. A strong aqueous solution of hydroxylamine hydrochloride (1.5 mols.) was then added and the mixture allowed to stand at ordinary temperature. Hydrogen sulphide was evolved in small amount and finally this pyrimidine deposited in the form of colorless prisms arranged in burrs. The yield of crude material was 2.5 grams, or 96.1 per cent. of the theoretical. This pyrimidine is insoluble in absolute alcohol and cold water. It possesses the characteristic property of crystallizing from hot water in two crystalline modifications. On slow cooling and in not too concentrated solution it deposits in beautiful, stout blocks, while in very concentrated solutions and when cooled quickly it separates as prisms arranged in sheaves. Both forms were free from sulphur and melted at 225°–228° with violent effervescence. This

melting point, however, varies according to the mode of heating. The pyrimidine gives no precipitate with picric acid or platinum chloride solution. It contains water of crystallization which was determined by heating at 130°–140°.

I. 0.4751 gram substance lost 0.0301 gram H_2O.

Nitrogen determinations (Kjeldahl):

	Calculated for $C_5H_7O_2N_3 \cdot \frac{1}{2}H_2O$	Found
H_2O	6.0	6.3
N	28.0	28.2, 28.3, 28.37, 28.1, 28.05, 28.38

Experiment 2

α-Oximido-β-mercaptopropionic Acid (Oxime of Mercaptopyruvic Acid, $HS.CH_2.C(:NOH)COOH$.—In this experiment we used 5 grams of 4-methyl-6-oxypyrimidine-2-oxalothioglycollic acid, 3 molecular proportions of hydroxylamine hydrochloride (4 grams) and 5 molecular proportions of sodium hydroxide (3.8 grams). The procedure was then exactly the same as in our first experiment. In this experiment, however, within one-half hour we obtained a magma of colorless needles. No attempt was made to identify this substance, but the mixture was allowed to stand at ordinary temperature. Within a few hours this crystalline material began to disappear, carbon dioxide was slowly evolved and finally balls of minute prisms began to form and deposit on the bottom of the flask. In about 5 days the transformation was complete and only the balls remained suspended in the liquid. This crystalline substance was identified as 2-oximido-4-methyl-6-oxypyrimidine described in the previous experiment. It exhibited the same characteristic behavior when recrystallized from hot water and decomposed with effervescence at 225°–228°. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_2N_3 \cdot \frac{1}{2}H_2O$	Found
N	28.0	28.1

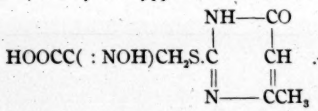
The aqueous filtrate (above) was carefully acidified with hydrochloric acid, when the oximidomercaptopropionic acid

deposited in corpuscular crystals. The material contained sulphur and melted without further purification at 172°–173° with effervescence. The acid crystallizes from hot water in needlelike prisms, which decompose at 178°–180° with charring and effervescence. Analysis (Kjeldahl):

	Calculated for $C_5H_5O_3NS$	Found
N	10.37	10.13

Experiment 3

4-Methyl-6-oxypyrimidine-2-oximidothiopropionic Acid,



HOOCC(: NOH)CH_2S.C CH .—In this experiment we

N—— CCH_3

used 15 grams of 4-methyl-6-oxypyrimidine-2-oxalothioglycollic acid and subjected it to exactly the same treatment as in Experiment 2. There was an immediate reaction and within 30 minutes a magma of colorless needles was obtained. These were separated by filtration and dried in a desiccator over sulphuric acid (filtrate saved). This substance was a sodium salt and decomposed at 195°–200° with effervescence. It was not analyzed. The salt was very soluble in cold water and on adding hydrochloric acid to the aqueous solution the oximido acid deposited at once. This acid was purified by crystallization from boiling absolute alcohol and separated, on cooling, in clusters of prisms which melted at 160°–161° with effervescence. This melting point, however, varies according to the mode of heating. If heated slowly in a sulphuric acid bath the acid will decompose at about 150°. This compound exhibits pyro-electric properties. The yield of crude acid was 6.5 grams. Analyses (Kjeldahl):

	Calculated for $C_6H_9O_4N_2S$	Found	
		I	II
N	17.28	17.10	17.22

The aqueous filtrate (above) was allowed to stand at ordinary temperature, when a small amount of 2-oximido-4-methyl-

6-oxypyrimidine separated. It melted after one crystallization from water at 225°–228°. Analysis (Kjeldahl):

	Calculated for $C_5H_7O_2N_3 \cdot \frac{1}{2}H_2O$	Found
N	28.0	28.3

After separating the above oxime the aqueous filtrate was then acidified with dilute hydrochloric acid, when there was a slight evolution of hydrogen sulphide and α-oximido-β-mercaptopropionic acid separated. The crude acid melted at 174°–175°. The yield was small.

Experiment 4.

Sodium Salt of 4-Methyl-6-oxypyrimidine-2-oximidothiosuccinic Acid, $NaOOC.CH(NOH)C(=N)NH\text{—}CO\text{—}C(=CH)CH_3$.—In this experiment we used the following proportions: 5 grams of the oxalothioglycollic acid, 3 grams of sodium hydroxide (4 mols.) and 1.3 grams of hydroxylamine hydrochloride (1 mol.). Otherwise the procedure was the same as in the preceding experiments. After standing for about 30 hours, the solution was then acidified (cold) with dilute hydrochloric acid. This sodium salt deposited at once as a colorless powder. It was separated, washed and then dried in a desiccator. It was soluble in water and insoluble in alcohol. It decomposed at about 200° with effervescence. Nitrogen determination (Kjeldahl):

	Calculated for $C_9H_7O_6N_3SNa_2$	Found
N	12.6	12.42

An attempt to prepare the pure oximido acid from this salt was unsuccessful. The salt was dissolved in water and the solution acidified strongly with hydrochloric acid, when a colorless crystalline substance separated, which decomposed with violent effervescence at 153°–155°. The yield was 2 grams and a nitrogen determination on the crude material indicated a mixture of the oxime of the dibasic acid and 4-methyl-

6-oxypyrimidine-2-oximidothiopropionic acid. We found 15.7 per cent. of nitrogen while the calculated value for the dibasic acid is 17.28 per cent., and that for the monobasic acid is 14.6 per cent. After crystallization from alcohol the pure oxime of the monobasic acid (previously described) separated in clusters of prisms and decomposed at 158° with effervescence. Analysis (Kjeldahl):

	Calculated for $C_8H_9O_4N_3S$	Found
N	17.28	17.4

In a fifth experiment in which 3 molecular proportions of hydroxylamine hydrochloride and 5 proportions of sodium hydroxide were used we obtained not only the α-oximido-β-mercaptopropionic acid in good yield, but also succeeded in isolating as by-products small amounts of 2-thio-4-methyluracil and 4-methyluracil.

The Action of Hydroxylamine on 4-Methyl-6-oxypyrimidine-2-thiopyruvic Acid

Two and one-half grams of pyruvic acid and 2 grams of potassium hydroxide (3 mols.) were dissolved in cold water and 2 molecular proportions of hydroxylamine hydrochloride added to the solution. The mixture was then allowed to stand for about 4.5 hours, when the reaction was apparently complete. 2-Oximido-4-methyl-6-oxypyrimidine had separated and was purified by crystallization from hot water. It melted at 225°–228° with violent effervescence and the yield was practically quantitative.

The filtrate above, which was neutral to turmeric and litmus, was acidified with hydrochloric acid, when we obtained an immediate precipitate. The substance was identified as α-oximido-β-mercaptopropionic acid and melted at 178°–180° with effervescence. A mixture of this substance and some of the oximido acid prepared in Experiment 2 above melted at the same temperature. It contained sulphur, but was free from chlorine. Analysis (Kjeldahl):

	Calculated for $C_3H_5O_2NS$	Found
N	10.3	9.97

The Behavior of 4-Methyl-6-oxypyrimidine-2-oximidothiopropionic Acid, HOOCC(: NOH)$CH_2S(C_5H_5ON_2)$, on Reduction

I. Reduction with Stannous Chloride and Hydrochloric Acid.—Six grams of stannous chloride were dissolved in a mixture of 40 cc. of water and 20 cc. of dilute hydrochloric acid. Three grams of the oxime were then added and the acid heated to 55°–60°. The oxime dissolved, forming a light yellow solution, and hydrogen sulphide was slowly evolved. After heating for one hour at 50° the mixture was diluted with water and the tin precipitated as sulphide with hydrogen sulphide. After removal of the tin the filtrate was then evaporated to dryness by heating at 45°–50° under diminished pressure. We obtained a crystalline residue, which contained both chlorine and sulphur. The substance was insoluble in alcohol but dissolved in hot water and, on cooling, clusters of needles deposited, which decomposed when heated above 275°. This product contained no chlorine or sulphur and was identified as 4-methyluracil. The filtrate from the 4-methyluracil gave a strong test for chlorine, and, when made alkaline with dilute sodium hydroxide solution and warmed, ammonia was evolved. This result proved the presence of ammonium chloride, indicating that the oxime was hydrolyzed during the reduction and the hydroxylamine then reduced to ammonia. No other decomposition product was identified.

II. Reduction with Zinc Dust and Formic Acid.—Three grams of the oxime and an excess of zinc dust were suspended in 100 cc. of formic acid of specific gravity 1.2. The oxime slowly dissolved and hydrogen sulphide was evolved immediately. The reduction was continued for 5 days at ordinary temperature, when the mixture was diluted copiously with water and the excess of zinc precipitated with hydrogen sulphide. After filtering from undissolved zinc and the zinc sulphide, the solution was then evaporated to dryness, the residue dissolved in water and the last traces of zinc precipitated as sulphide. On evaporating the solution to dryness again we obtained a crystalline residue, which was purified by crystallization from boiling water. On cooling, flat prisms

separated, which did not melt or decompose below 280°. This substance contained sulphur and was identified as 2-thio-4-methyluracil. Analysis for sulphur (Carius):

I. 0.0908 gram substance gave 0.1520 gram $BaSO_4$.

	Calculated for $C_5H_6ON_2S$	Found
S	22.53	22.9

After the separation and purification of the methylthiouracil the filtrates were combined, concentrated and then subjected to the Baumann and Schotten reaction with 5 grams of benzoyl chloride and an excess of sodium bicarbonate. After the benzoyl chloride had disappeared the solution was acidified with hydrochloric acid, when a crystalline precipitate was obtained. This was separated, dried and then digested with ligroin to remove benzoic acid. We obtained a small amount of insoluble material, which was purified by crystallization from hot water. It separated, on cooling, in prisms, which were badly etched and melted at 163°–165°. This melting point indicated that we were dealing with benzoylalanine. Fischer[1] states that this acid melts at 165°–166°. We did not obtain enough of the pure acid for analysis.

III. Reduction with Aluminium Amalgam.—In this experiment the oxime was dissolved in about 90 per cent. alcohol and an excess of aluminium amalgam suspended in the solution. The reduction was continued for two days. Hydrogen sulphide was slowly generated. After filtering from aluminium hydroxide the filtrate was evaporated to dryness, when a crystalline residue was obtained. This was first triturated with cold, dilute hydrochloric acid to remove any base present and the insoluble material purified by crystallization from hot water. The product that separated here appeared to be a mixture of 4-methyluracil and 4-methyl-2-thiouracil. By repeated recrystallizations from water the thiouracil was finally separated sufficiently pure for analysis. It did not melt below 300° and a nitrogen determination (Kjeldahl) gave:

	Calculated for $C_5H_6ON_2S$	Found
N	19.7	19.36

[1] Ber. d. chem. Ges., **33**, 2454.

When the hydrochloric acid solution above was evaporated a syrupy residue was obtained. This was shaken with benzoyl chloride and alkali but we did not succeed in isolating any benzoylalanine.

Reduction of 2-Oximido-4-methyl-6-oxypyrimidine

One gram of the oxime and 2 grams of crystalline stannous chloride were dissolved in dilute hydrochloric acid and the solution heated on the steam bath for 30 minutes. The solution was then evaporated to dryness to remove hydrochloric acid, the residue dissolved in water and the tin precipitated with hydrogen sulphide. After filtering off the tin sulphide the solution was concentrated and cooled, when 4-methyluracil separated. We obtained no evidence of the formation of 2-amino-4-methyl-6-oxypyrimidine, the oximido group having been detached as hydroxylamine. Analysis (Kjeldahl):

	Calculated for $C_5H_6O_2N_2$	Found
N	22.2	21.95

The Action of Hydroxylamine on Diethyl 4-Methyl-6-oxypyrimidine-2-oxalothioglycollate

Three molecular proportions of potassium hydroxide (5 grams) were dissolved in water and 10 grams of this pyrimidine dissolved in the cold alkali solution. Two molecular proportions of hydroxylamine hydrochloride were then added and the solution allowed to stand for 1.5 hours at ordinary temperature. A yellow solid had then deposited and was separated by filtration and the filtrate allowed to stand. The weight of this crystalline substance was 1.5 grams and it was identified as ethyl 4-methyl-6-oxypyrimidine-2-thioglycollate. It crystallized from alcohol in prisms and melted at 146° to a clear oil. The original solution, after standing about 12 hours longer, deposited 3.5 grams more of a crystalline substance. This was purified by crystallization from hot water and was identified as 2-oximido-4-methyl-6-oxypyrimidine. It melted at 224°–227° and a mixture of the compound with some of the pure oxime melted at the same temperature.

The Behavior of the α-Oximido-β-mercaptopropionic Acid, $HSCH_2.C(:NOH)COOH$, on Reduction

This compound undergoes complete decomposition in the presence of reducing agents and we obtained no evidence of the formation of cysteine or cystine. We used tin chloride, aluminium amalgam and zinc and formic acid, but in every case hydrogen sulphide was evolved immediately at ordinary temperature. We also did not observe a smooth formation of alanine. Not only is hydrogen sulphide evolved in the presence of reducing agents but the oxime undergoes hydrolysis with formation of hydroxylamine, which is then reduced to ammonia. The following experiment was performed with zinc and formic acid as the reducing agent: Five grams of the oximido acid and an excess of zinc dust were suspended in a mixture of 150 cc. of formic acid of specific gravity 1.2 and 50 cc. of specific gravity 1.12. Hydrogen sulphide was evolved immediately at ordinary temperature. After standing about 24 hours at ordinary temperature the mixture was then warmed on the steam bath for 5 hours and finally transferred to an evaporating dish and diluted copiously with alcohol. The alcohol and formic acid were then evaporated, the residue left behind triturated with warm water and an insoluble residue filtered off. This was identified as zinc sulphide. The filtrate was saturated with hydrogen sulphide to remove the zinc as sulphide, filtered and again evaporated to dryness after acidifying with hydrochloric acid. We obtained a crystalline deposit which contained a large amount of ammonium chloride. The ammonia was expelled by digestion with barium hydroxide solution, the barium precipitated by addition of the required amount of sulphuric acid and the solution then evaporated to dryness. We thus obtained about 1.5 grams of a partially crystalline residue, which was colorless and very soluble in water. This was dried at 100° and then warmed at 100°, in about 6 cc. of acetic anhydride, with 2.7 grams of potassium thiocyanate. There was an immediate reaction on warming, the solution assumed a red color and free thiocyanic acid was evolved. After heating for about 15 minutes and then pouring into cold water a viscous oil separated which

finally solidified on standing. This was a very impure substance but finally a small amount of crystalline material was separated by crystallization from alcohol. It melted at 165°–168°, and gave a strong test for sulphur. We did not obtain enough of this substance for analysis but it was probably 2-thio-3-acetyl-4-methylhydantoin.[1]

NEW HAVEN, CONN.
July 2, 1912

[Contributions from the Sheffield Laboratory of Yale University]

CCIII.—RESEARCHES ON PYRIMIDINES
THE ACTION OF POTASSIUM THIOCYANATE ON PRIMARY HALIDES[2]

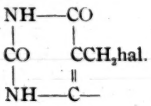
BY TREAT B. JOHNSON AND ARTHUR J. HILL

[FIFTY-SEVENTH PAPER]

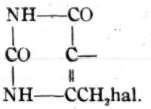
In the acyclic series an unsaturated condition in the 2,3-position of a halide $\overset{3}{C} : \overset{2}{C}.\overset{1}{CH}.$ hal.— is favorable to the formation of an isothiocyanate, —NCS. For example, allyl iodide reacts with potassium thiocyanate to form the corresponding isothiocyanate or allyl mustard oil (I). Only a small number of such halides have been investigated, but, so far as examined, it is not possible to isolate the primary products of the reaction, *thiocyanates*, unless heat is avoided. We have also observed this same characteristic behavior when this unsaturated grouping functionates in the halides of the cyclic series. The pyrimidine imidechlorides corresponding to the formula $\underset{\llcorner\!\!_\!\!_\!\!_

cyanate. We found, however, in some cases that the primary thiocyanates possessed remarkable stability and could be isolated and easily purified without rearrangement at ordinary temperature. In fact, these cases of molecular rearrangement, in the pyrimidine series, were unique for this type of change.

Two interesting types of pyrimidine halides, which have not been studied, are the halide derivatives of 4- and 5-methyldiketotetrahydropyrimidines, which may be represented by the formulas (II) and (III). The chemical evidence, so far obtained, indicates that these ketopyrimidines contain their double bond between the 4- and 5-positions of the ring. Therefore, their corresponding primary halides, (II) and (III), theoretically should react with potassium thiocyanate to form isothiocyanates. The primary object of the work described in this paper was to test this assumption. We shall give a description of the synthesis and behavior towards potassium thiocyanate of a primary halide corresponding to Type (III).



II

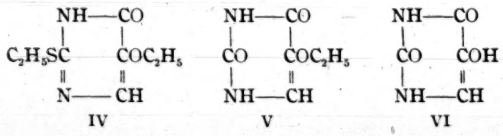


III

During the progress of an investigation by Mr. Hill on the mechanism of Claisen's condensation, we had occasion to investigate the action of metallic sodium on ethyl phenoxyacetate, $C_6H_5OCH_2COOC_2H_5$. We observed that the ester undergoes a normal condensation with formation of the sodium salt of ethyl α,γ-diphenoxyacetoacetate (IX). Ethyl β-naphthoxyacetate behaves in a similar manner, forming the sodium salt (XVIII). The yields of these two salts, however, were small, owing, apparently, to secondary reactions. We have now found unexpectedly that these condensations are influenced by the presence of certain reagents, which act catalytically. The yields of the salts (IX) and (XVIII) are thereby greatly increased and consequently we have been able to ob-

tain them in sufficient quantity for experimental purposes.[1]

We have investigated the action of both of these salts on thiourea and find that they condense smoothly with formation of the corresponding pyrimidines, viz., 2-thio-4-phenoxymethyl-5-phenoxy-6-oxypyrimidine (XI) and 2-thio-4-naphthoxymethyl-5-naphthoxy-6-oxypyrimidine (XVI), respectively. Both pyrimidines are desulphurized quantitatively by digestion with chloroacetic acid, in aqueous solution, forming the corresponding diphenoxy- and dinaphthoxypyrimidines, (XII) and (XVII), respectively. Attempts to desulphurize these thiopyrimidines by alkylation and then hydrolysis of their corresponding mercapto derivatives, (X) and (XIII), were unsuccessful. The mercaptopyrimidines could be boiled with hydrochloric and hydrobromic acids for hours without decomposition. This behavior is in accord with previous observations. Johnson and McCollum,[2] for example, observed that the ethyl ether of isobarbituric acid (V) cannot be obtained by boiling 2-ethylmercapto-5-ethoxy-6-oxypyrimidine (IV) with hydrochloric or hydrobromic acid. By heating with hydrochloric acid in a bomb tube at 150° a mixture of the ethoxypyrimidine and isobarbituric acid (VI) was obtained.



IV V VI

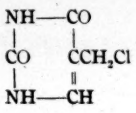
In a recent paper, Johnson and Guest[3] have given a description of 5-phenoxyuracil and have shown that the phenoxy group is so firmly bound that this pyrimidine can be heated with hydrochloric acid at 160° without change. It was therefore of special interest to investigate the action of hydrochloric acid on the diphenoxypyrimidine (XII). We now find that the 5-phenoxy group, in this compound, is as firmly bound

[1] We shall describe in a future paper the results of our investigation on catalysis in Claisen's condensation.—T. B. J.

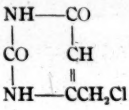
[2] J. Biol. Chem., **1**, 437.

[3] This Journal, **42**, 272.

as that in 5-phenoxyuracil. On the other hand, the aliphatic grouping $—CH_2OC_6H_5$ in position 4 undergoes hydrolysis by the action of hydrochloric acid and the diphenoxypyrimidine (XII) is transformed into the chloropyrimidine (XV) with formation of carbolic acid. An attempt to effect an analogous change with the dinaphthoxypyrimidine (XVII) was unsuccessful and only amorphous products of indefinite composition were obtained. Since the methyl groups in thymine and 4-methyluracil are not attacked by the halogens, therefore this reaction is of particular interest and we hope to be able to apply it later and synthesize the unknown chloro derivatives, (VII and VIII), of these two pyrimidines. These halides should be of value for further interesting syntheses.

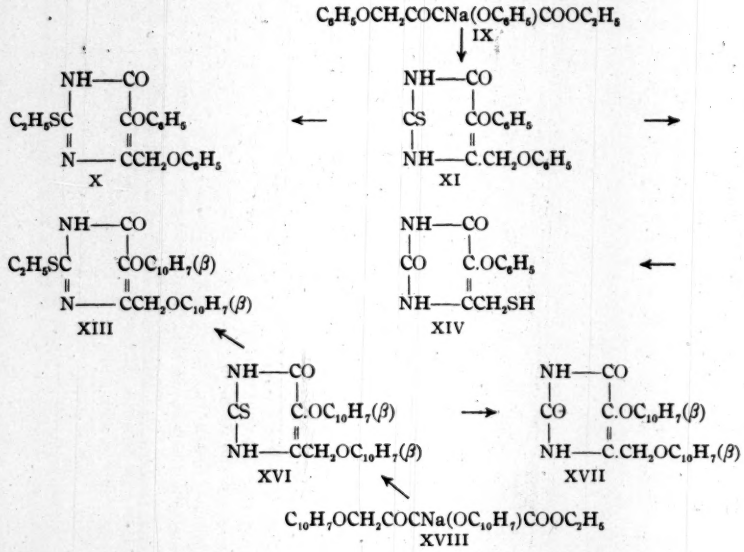


VII

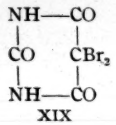


VIII

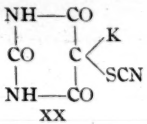
We have now made the interesting observation that this chloropyrimidine (XV), which contains the same unsaturated grouping as is present in allyl chloride, $—C : C.CH_2Cl$, reacts with potassium thiocyanate in an abnormal manner. The product of the reaction is neither a thiocyanate nor an isothiocyanate, but the mercaptopyrimidine (XIV). The thiocyanate is apparently the primary product of the reaction, but, instead of rearranging to an isothiocyanate, it loses its cyanogen radical and a mercaptan is formed. So far as the writer is aware this is the first case where it has been observed that a primary halide can react with potassium thiocyanate, in an alcoholic solution, in this unique manner with formation of a mercaptan. It is especially interesting that we should observe this behavior with a halide containing a grouping favorable for the formation of an isothiocyanate. These various transformations are represented by the following formulas:


C6H5OCH2COCNa(OC6H5)COOC2H5
IX
NH—CO
CS C.OC6H5
NH—C.CH2OC6H5
XI
NH—CO
C2H5SC COC6H5
N— CCH2OC6H5
X
NH—CO
CO C.OC6H5
NH—C.CH2OC6H5
XII
NH—CO
CO C.OC6H5
NH—CCH2Cl
XV
NH—CO
CO C.OC6H5
NH—CCH2SH
XIV
NH—CO
C2H5SC COC10H7(β)
N— CCH2OC10H7(β)
XIII
NH—CO
CS C.OC10H7(β)
NH—CCH2OC10H7(β)
XVI
NH—CO
CO C.OC10H7(β)
NH—C.CH2OC10H7(β)
XVII
C10H7OCH2COCNa(OC10H7)COOC2H5
XVIII

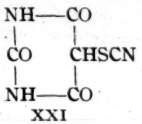
Regarding the mechanism of this unique change, we have no decisive evidence, but it is apparently analogous to that involved in the transformation of thiocyanobarbituric acid (XXI) into thiodialuric acid (XXII). Trzcinski[1] prepared the potassium salt of this interesting thiocyanate (XX) by the action of potassium thiocyanate on dibromobarbituric acid (XIX), but he was unable to isolate the free thiocyanate because of its instability. He writes as follows regarding the properties of this thiocyanate: "Vermischt man concentrirte Lösungen ihrer Salze mit überschüssiger Salzsäure, so entsteht ein krystallinischer, in Wasser löslicher Niederschlag, der sich aber nicht unkrystallisiren lässt, indem er, schon gelinde mit Wasser erwärmt, sich zersetzt, wobei Sulfodialursäure, Blausäure, Sulfocyansäure und ein in Alkalien und Säuren unloslicher Körper entstehen."



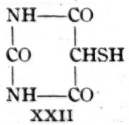
XIX



XX



XXI



XXII

The study of chloropyrimidines containing the grouping —C : C.CH_2Cl will be continued.

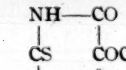
EXPERIMENTAL PART

Sodium Salt of Ethyl α,γ-Diphenoxyacetoacetate, $C_6H_5OCH_2COCNa(OC_6H_5)COOC_2H_5$.—This salt was obtained by the molecular condensation of ethyl phenoxyacetate in ether solution and in presence of the required amount of metallic sodium. The sodium gradually dissolved and the salt deposited as a light colored granular powder. The yield of

[1] Ber. d. chem. Ges., **16**, 1060.

salt from 25 grams of ethyl phenoxyacetate was 18 grams. This crude salt was used for the preparation of

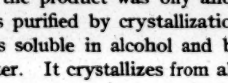
2-Thio-4-phenoxymethyl-5-phenoxy-6-oxypyrimidine,



.—Calculating that the sodium salt (18 grams) was pure, molecular proportions of sodium and thiourea were dissolved in absolute alcohol and the sodium salt suspended in the solution. After heating on the steam bath for about 10 hours the condensation was considered complete and the excess of alcohol evaporated. The residue was then dissolved in a small volume of water and hydrochloric acid added cautiously, when hydrogen sulphide was evolved and this pyrimidine separated in a crystalline condition. Sometimes the product was oily and slowly hardened on cooling. It was purified by crystallization from alcohol. The pyrimidine is soluble in alcohol and benzene and difficultly soluble in water. It crystallizes from alcohol in slender prisms, which melt at 218° to a red oil. The yield was 8 grams. Analysis (Kjeldahl):

	Calculated for $C_{17}H_{14}O_3N_2S$	Found
N	8.58	8.30

2-Ethylmercapto-4-phenoxymethyl-5-phenoxy-6-oxypyrimidine,



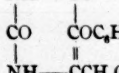
.—Six-tenths of a gram of sodium was dissolved in alcohol and 8 grams of the preceding 2-thiopyrimidine dissolved in the solution by warming on the steam bath. Six and five-tenths grams of ethyl iodide were then added and the solution heated for about 30 minutes at 100°, when it was neutral. The alcohol and excess of iodide were then evaporated and the crude mercaptopyrimidine triturated with water to remove sodium iodide. The pyrimidine was purified by crystallization from alcohol and melted

at 170°. It crystallizes in characteristic, hexagonal prisms, which are insoluble in water and quite soluble in benzene. Analyses (Kjeldahl):

	Calculated for $C_{19}H_{18}O_3N_2S$	Found I	Found II
N	7.90	7.74	7.86

Attempts to hydrolyze this mercaptopyrimidine to 2,6-dioxy-4-phenoxymethyl-5-phenoxypyrimidine were unsuccessful. It was recovered unaltered after long digestion with hydrochloric and hydrobromic acids.

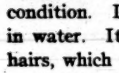
2,6-Dioxy-4-phenoxymethyl-5-phenoxypyrimidine,



.—This pyrimidine was formed by digesting the corresponding 2-thiopyrimidine with a strong aqueous solution of chloroacetic acid. The thio compound dissolved on boiling and finally, when the desulphurization was complete, this pyrimidine separated from the hot solution in a crystalline condition. It is soluble in benzene and alcohol and insoluble in water. It crystallizes from alcohol in distorted needles or hairs, which melt at 200°. It did not contain sulphur. Analyses (Kjeldahl):

	Calculated for $C_{17}H_{14}O_4N_2$	Found I	Found II
N	9.03	9.15	9.15

2,6-Dioxy-4-chloromethyl-5-phenoxypyrimidine,

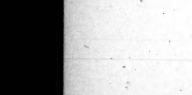


.—This pyrimidine was obtained by heating the above diphenoxypyrimidine with hydrochloric acid. The transformation, however, is not smooth and considerable resinous material is formed during the reaction. After several preliminary experiments it was finally found that the best yield of chloropyrimidine was obtained under the following conditions: Five grams of 2,6-dioxy-4-phenoxymethyl-5-phenoxypyrimidine were heated with 25 cc. of concentrated

hydrochloric acid, in a bomb tube, for 5 hours, at 140°–150°. A dark solution was obtained and some resinous substance was suspended in the fluid. The contents of the tube were evaporated on the steam bath when a resinous residue was obtained. We then triturated this with warm water, when it finally congealed to an amorphous product, which was soluble in warm alcohol. On cooling, this chloropyrimidine separated in characteristic, square plates, which melted at 248°. It gave a strong test for chlorine. The compound is soluble in alcohol and hot water and insoluble in benzene. Analyses (Kjeldahl):

	Calculated for $C_{11}H_9O_3N_2Cl$	Found I	Found II
N	11.09	11.05	11.02

2,6-Dioxy-4-mercaptomethyl-5-phenoxypyrimidine,



.—Two grams of 2,6-dioxy-4-chloromethyl-5-phenoxypyrimidine and one gram of dry potassium thiocyanate were dissolved in alcohol and the solution heated on the steam bath for 5–6 hours. Potassium chloride deposited on the sides of the flask. The solution was evaporated to remove all alcohol, when we obtained an oil which finally solidified on cooling. After trituration with water to dissolve potassium chloride and potassium thiocyanate the compound was purified by crystallization from alcohol. It separated from this solvent in needles, which decomposed at 182°. This decomposition point is very characteristic. The compound shrivels abruptly, forming a resin, at 182°, and then decomposes as the temperature is raised. It gave a strong test for sulphur. Analyses:

Nitrogen determination (Kjeldahl).

Sulphur determination (Carius).

I. 0.1468 gram substance gave 0.1329 gram $BaSO_4$.

	Calculated for $C_{11}H_{10}O_3N_2S$	Found I	Found II	Found III
N	11.2	10.65	11.12	...
S	12.8	...	...	12.43

Sodium Salt of Ethyl α,α-Dinaphthoxyacetoacetate, $C_{10}H_7OCH_2COCNa(OC_{10}H_7)COOC_2H_5$.—This salt was obtained by the molecular condensation of ethyl β-naphthoxyacetate[1] in the presence of the required amount of sodium. The salt was obtained as a granular powder but the yield was poorer than in the case of the corresponding phenoxy derivative. No attempt was made to isolate the ketone ester and we used the crude salt for the preparation of the following pyrimidine:

2-Thio-4-naphthoxymethyl-5-naphthoxy-6-oxypyrimidine,

.—Sixty-five hundredths of a gram of sodium was dissolved in absolute alcohol and 12.8 grams of the crude sodium salt (above) and 3.2 grams of thiourea suspended in the solution. The mixture was then heated at 100° for ten hours and the alcohol evaporated. The residue was dissolved in the smallest volume of water possible and the solution acidified with hydrochloric acid. Hydrogen sulphide was evolved and this thiopyrimidine separated. The compound is insoluble in water and difficultly soluble in alcohol. It crystallizes from hot alcohol in characteristic, rhombic tables or plates, which melt at 224°–226° to a red oil. Analysis (Kjeldahl):

	Calculated for $C_{25}H_{18}O_3N_2S$	Found
N	6.57	6.54

2-Ethylmercapto-4-naphthoxymethyl-5-naphthoxy-6-oxypyrimidine, $C_2H_5S.C_{25}H_{17}O_3N_2$.—This mercaptopyrimidine was formed by alkylation of the preceding 2-thiopyrimidine with ethyl bromide in the presence of sodium ethylate. It is insoluble in water and soluble in benzene and alcohol. It was purified by crystallization from alcohol and crystallized in sheaves of needles melting at 198°. The mercapto group is

[1] *Loc. cit.*

not removed by digestion with concentrated hydrochloric or hydrobromic acid. Analysis (Kjeldahl):

	Calculated for $C_{27}H_{22}O_4N_2S$	Found
N	6.16	6.30

2,6-Dioxy-4-naphthoxymethyl-5-naphthoxypyrimidine,

.—Five grams of 2-thio-4-naphthoxymethyl-5-naphthoxy-6-oxypyrimidine were suspended in a concentrated aqueous solution of chloroacetic acid and the mixture heated to boiling for 7 hours. The thiopyrimidine finally completely dissolved and then this desulphurized product separated from the hot solution. The yield was quantitative. The pyrimidine was purified by crystallization from absolute alcohol and separated in minute needles arranged in clusters. Oftentimes it deposited in an amorphous state resembling freshly precipitated aluminium hydroxide. It was free from sulphur and melted at 256°–258° to a red oil. It is insoluble in water and benzene. Analysis (Kjeldahl):

	Calculated for $C_{29}H_{18}O_4N_2$	Found
N	6.83	7.09

Attempts to convert this dinaphthoxypyrimidine into 2,6-dioxy-4-chloromethyl-5-naphthoxypyrimidine were unsuccessful. It was heated with concentrated hydrochloric acid at different temperatures, but in every case products of a tarry nature were obtained and a pure chloro compound could not be isolated. Nitrogen and chlorine determinations in the purest product obtainable gave 6.9 per cent. for nitrogen and 1.5 per cent. for chlorine, while the calculated values for the pure chloropyrimidine are 9.2 per cent. and 11.2 per cent., respectively.

NEW HAVEN, CONN.
July 1, 1912

[Contributions from the Sheffield Laboratory of Yale University]

CCIV.—RESEARCHES ON PYRIMIDINES

THE OXIMES OF SOME THIOGLYCOLLIDE COMPOUNDS AND THEIR BEHAVIOR ON REDUCTION[1]

By Treat B. Johnson and Robert C. Moran

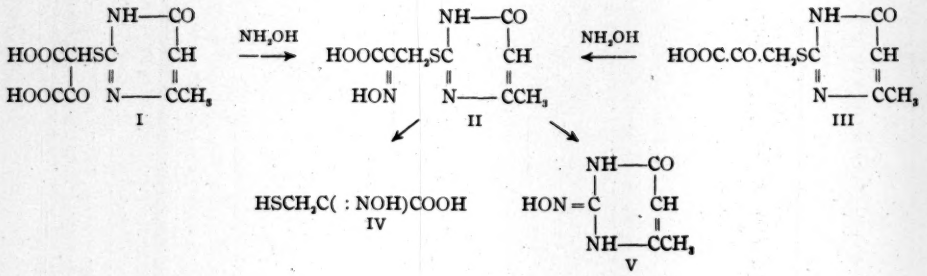
[FIFTY-EIGHTH PAPER]

In a preceding publication from this laboratory,[2] Johnson and Shepard have described a synthesis of the oxime of mercaptopyruvic acid or α-oximido-β-mercaptopropionic acid (IV). It was obtained by the action of hydroxylamine on 4-methyl-6-oxypyrimidine-2-oxalothioglycollic acid (I) or 4-methyl-6-oxypyrimidine-2-thiopyruvic acid (III). The product of the reaction, in both cases, was the oxime of the pyruvic acid (II), which then reacted with an excess of the hydroxylamine, forming the oxime of mercaptopyruvic acid (IV) and 2-oximido-4-methyl-6-oxypyrimidine (V). The various changes involved in this synthesis are represented by the following formulas.

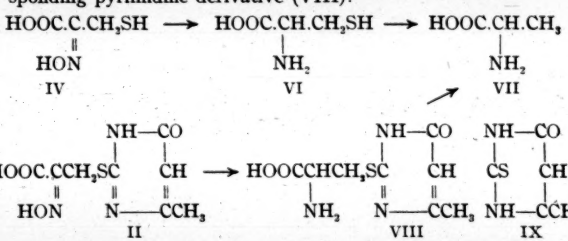
These two oximes, (IV) and (II), represent new types of sulphur compounds and naturally were of interest to us because of the possibility of their conversion, by reduction, into the corresponding amino acids. All attempts, however, to effect this change were unsuccessful. We found, on the other hand, that these two acids were extremely unstable in the presence of reducing agents and underwent partial hydrolysis with regeneration of hydroxylamine. The oximido groups were likewise reduced as expected, but, much to our surprise, the sulphur was also detached from the aliphatic residue with formation of alanine (VII), hydrogen sulphide and 2-thio-4-methyl-6-oxypyrimidine (IX). In other words, we obtained

[1] By the terms *thioglycollide* and *glycollide* are meant the groupings —S.CH_2.CO— and —O.CH_2.CO—, respectively, corresponding to the *polypeptide* grouping —NH . CH_2.CO—.—T. B. J.

[2] This Journal, **48**, 279.


NH—CO
HOOCCHSC CH
HOOCCO N— CCH3
I
NH2OH
NH—CO
HOOCCCH2SC CH
HON N— CCH3
II
NH2OH
NH—CO
HOOC.CO.CH2SC CH
N— CCH3
III
HSCH2C(: NOH)COOH
IV
NH—CO
HON=C CH
NH—CCH3
V

no evidence of the formation of cysteine (VI) or the corresponding pyrimidine derivative (VIII).



The behavior of these oximido acids on reduction was so unexpected and unique that it was of interest to examine another series of oximes containing the grouping

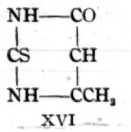
$$HON : \overset{|}{C}.CH_2S—$$

It was desirable to determine whether it is a characteristic property of compounds containing this linking to undergo reduction in this manner, or whether this behavior is due, in this case, to the presence of the carboxyl group of the oximido acid. In this paper we shall describe some representatives of a class of oximes containing the same grouping, but in which the carboxyl group of the above oximido acids is replaced by an aryl or alkyl group.

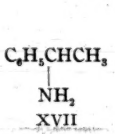
In the present investigation the starting point was 2-thio-4-methyl-6-oxypyrimidine.[1] This was converted into its sodium salt (X) and the latter then digested with monochloroacetone and bromoacetophenone, when the two pyrimidines, 2-acetylmethylmercapto-4-methyl-6-oxypyrimidine (XI) and 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine (XII), respectively, were obtained in excellent yields. Both of these ketones reacted smoothly with hydroxylamine, forming the corresponding oximes, (XIII) and (XV), respectively. We did not observe the formation of stereoisomeric modifications. We also prepared the hydrazone of 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine (XIV).

[1] List: Ann. Chem. (Liebig), **238**, 12.

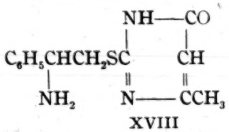
We have examined the behavior, towards reducing agents, of the oxime (XV) and hydrazone (XIV) of 2-benzoylmethyl-mercapto-4-methyl-6-oxypyrimidine. The oxime was reduced with ferrous sulphate and ammonia, with formic acid and zinc dust and with sodium amalgam. In every case we obtained 2-thio-4-methyl-6-oxypyrimidine (XVI). In the experiment in which sodium amalgam was used, we also succeeded in isolating phenylethylamine (XVII). This combined with phenyl isothiocyanate, giving methyldiphenylthiourea (XIX), which has been described by Michaelis and Linow.[1] We obtained no evidence of the formation of the amine (XVIII). Attempts to prepare this amine by reduction of the hydrazone (XIV) with sodium amalgam and aluminium amalgam were likewise unsuccessful. The only product which was identified was 2-thio-4-methyl-6-oxypyrimidine (XVI). The ketone (XII) was reduced by aluminium amalgam, in an alcoholic solution, forming 2-thio-4-methyl-6-oxypyrimidine (XVI) and apparently acetophenone.



XVI



XVII

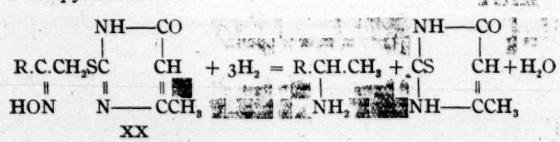


XVIII

XIX

Summary

Oximes of the general formula (XX) (R = CH_3, C_6H_5, COOH) are converted by reducing agents into amines and 2-thiopyrimidines.

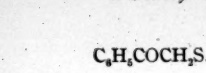


XX

[1] Ber. d. chem. Ges., 36, 2168.

EXPERIMENTAL PART

2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine,

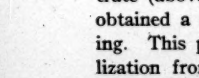


.—This pyrimidine is formed smoothly by the action of bromoacetophenone on the sodium salt of 2-thio-4-methyluracil. The dry sodium salt (20 grams) was suspended in 100 cc. of absolute alcohol and one molecular proportion of the bromide added (24.3 grams). On warming on the steam bath, there was an immediate reaction, the sodium salt dissolved and sodium bromide deposited. After digesting for about 3 hours the reaction was complete and the solution was neutral to turmeric and litmus. The solution was then cooled, when the above pyrimidine separated in well developed prisms mixed with sodium bromide. The pyrimidine was purified by first washing with cold water to remove sodium bromide and by recrystallization from alcohol. It crystallized, on cooling, in colorless prismatic crystals, which melted at 175° to an oil without decomposition. The yield of pure pyrimidine was 19.1 grams. The pyrimidine is soluble in dilute sodium hydroxide solution and insoluble in water. Analysis (Kjeldahl):

	Calculated for $C_{19}H_{17}O_3N_2S$	Found
N	10.72	10.70

After filtering from the mercaptopyrimidine the alcohol filtrate (above) was concentrated on the steam bath, when we obtained a syrupy residue, which deposited crystals on cooling. This product was separated and purified by recrystallization from hot alcohol. It was more soluble in alcohol than the pyrimidine and separated, on cooling, in prisms which melted at 118°–119° to a clear oil without effervescence. It was identified as

2-Benzoylmethylmercapto-4-methyl-6-benzoylmethoxypyrimidine,



.—This same com-

pound was also obtained by digesting, in alcohol, the sodium salt of 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine (see below) with the required amount of bromoacetophenone. The compound is formed smoothly in this manner and after concentration of the alcohol solution it separated in beautiful, prismatic crystals, which melted at 118°–119° to a clear oil. The constitution of the pyrimidine is established by the facts that it is not soluble in sodium hydroxide solution and is converted into 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine by hydrolysis with acids. Analysis (Kjeldahl):

	Calculated for $C_{21}H_{18}O_3N_2S$	Found
N	7.40	7.40

Hydrolysis with Hydrochloric Acid.—One gram of the above pyrimidine was suspended in 60 cc. of concentrated hydrochloric acid and the mixture heated on the steam bath for just 10 minutes. We obtained a colorless solution which deposited, on cooling, a colorless crystalline substance. This was purified by crystallization from alcohol and separated in prisms, which melted at 175°. They contained sulphur and were identified as 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine. The latter pyrimidine on prolonged hydrolysis is finally converted into 4-methyluracil. For example: Two grams of the pyrimidine were suspended in 50 cc. of concentrated hydrochloric acid and the mixture boiled for about 1.5–2 hours. An oil was obtained, which solidified on cooling. This was separated and recrystallized from boiling alcohol. It separated, on cooling, in yellow prisms, which melted at 115° to an oil without decomposition. The substance gave a strong test for sulphur, but did not contain nitrogen. When some of the compound was placed in concentrated sulphuric acid it dissolved, giving a brilliant purple solution. This color was destroyed by dilution with water. The compound was not desulphurized by digestion in dilute alcoholic solution with silver nitrate, mercury oxide or lead acetate. Apparently this compound was not the mercaptan $C_6H_5COCH_2SH$ or its corresponding disulphide, $(C_6H_5COCH_2S)_2$. It is now being

investigated and the results obtained will be published in a later paper. Sulphur determination (Kjeldahl):

I. 0.3004 gram substance gave 0.07333 gram $BaSO_4$.

	Calculated for C_8H_8OS	Found
S	20.3	24.4

The acid filtrate (above) was evaporated to dryness and the residue dissolved in a small volume of hot water. On cooling methyluracil deposited. Analysis (Kjeldahl):

	Calculated for $C_5H_6O_2N_2$	Found
N	22.22	22.37

Sodium Salt of 2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine, $C_6H_5CO.CH_2S.C(=N-)CONa$ / $CH=C(-N=)CCH_3$.—Sixty-three hundredths of a gram of pure sodium hydroxide was dissolved in 15 cc. of cold water and 2 grams of the mercaptopyrimidine dissolved in the solution by gentle warming. On cooling, this salt separated in the form of needles. The compound shrivels when heated, in a capillary tube, above 100° and decomposes at 206° with effervescence. The weight of salt which separated was 1.9 grams. Analysis (Kjeldahl):

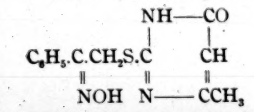
	Calculated for $C_{12}H_{11}O_2N_2SNa$	Found
N	9.93	9.90

2-Acetylmethylmercapto-4-methyl-6-oxypyrimidine, $CH_3COCH_2S.C(=N-)NH-CO$ / $CH=C(-N=)CCH_3$.—This pyrimidine was prepared by digestion of the sodium salt of 2-thio-4-methyluracil in alcohol with the required amount of chloroacetone. It was purified by recrystallization from hot alcohol and separated, on cooling, in slender needlelike prisms, which melted at 152° to a clear oil without decomposition. The pyrimidine is insoluble

in hot and cold water and soluble in sodium hydroxide solution. Analysis (Kjeldahl):

	Calculated for $C_5H_{10}O_2N_2S$	Found
N	14.14	14.4

Oxime of 2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine,



.—This oxime was prepared by the action of hydroxylamine on 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine in aqueous solution. Four grams of the pyrimidine and 1.23 grams of sodium hydroxide were dissolved in 25 cc. of water. To this cold solution were then added 1.07 grams of hydroxylamine hydrochloride dissolved in 5 cc. of water. The mixture was then allowed to stand at ordinary temperature for 10–12 hours when it had assumed a pale yellow color and a small amount of solid material had separated. This was separated by filtration and sufficient hydrochloric acid added to the filtrate to combine with the sodium. A slight amount of hydrogen sulphide was evolved and the oxime separated as a light yellow solid. It was dried in a desiccator over concentrated sulphuric acid. It was purified for analysis by recrystallization from alcohol and melted at 183° to a yellow oil with effervescence. The oxime dissolves in sodium hydroxide solution but is insoluble in water. While the oxime could be recrystallized in small quantities from alcohol, nevertheless attempts to purify large amounts in this manner were unsuccessful. It dissolves with some difficulty and the oxime is partially decomposed by long boiling, forming methyluracil. Analysis (Kjeldahl):

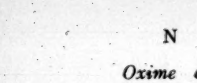
	Calculated for $C_{13}H_{13}O_2N_3S$	Found
N	15.27	15.30

Hydrochloride of the Oxime.—The oxime separated in the form of its hydrochloric acid salt when it was precipitated

from its alkaline solution by addition of an excess of hydrochloric acid. Analysis (Kjeldahl):

	Calculated for $C_{13}H_{13}O_2N_3S.HCl$	Found
N	13.48	13.31

Oxime of 2-Acetylmethylmercapto-4-methyl-6-oxypyrimidine,



.—While the oxime of 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine was formed in aqueous solution this oxime, on the other hand, did not form smoothly under similar conditions. It was therefore prepared as follows: The pyrimidine was dissolved in alcohol and this solution combined with an aqueous solution containing the required amount of hydroxylamine. On standing at ordinary temperature the oxime finally separated as a colorless solid. It was difficultly soluble in alcohol and was decomposed by warming with water, forming 2-acetylmethylmercapto-4-methyl-6-oxypyrimidine melting at 152°. The oxime melts at about 162° to an oil with decomposition. Analysis (Kjeldahl):

	Calculated for $C_8H_{11}O_3N_3S$	Found
N	19.71	19.3

Reduction of 2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine with Aluminium Amalgam.—Five grams of the pyrimidine were dissolved in 95 per cent. alcohol and about 10 grams of amalgamated aluminium suspended in the solution. The reduction was conducted in a flask and the latter was connected with a return condenser. The reaction was allowed to proceed for 10–12 hours when 5 cc. of water were added and the mixture then heated on the steam bath for 2 hours. The mixture was then cooled, the aluminium hydroxide and excess of amalgam separated by filtration and the alcohol filtrate concentrated on the steam bath. On cooling, a crystalline substance separated. This gave a strong test for sulphur and was identified as 2-thio-4-methyluracil. The alcohol filtrate

was concentrated still further and cooled again when the unaltered mercaptopyrimidine separated and melted at 175°.

Phenylhydrazone of 2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine, $C_6H_5C.CH_2SC(NH{-}CO)CH(N{-}CCH_3)C_6H_5NHN$.—This hydrazone was prepared by dissolving 2.5 grams of phenylhydrazine in 5 cc. of alcohol and then adding the solution to an alcoholic solution of the mercaptopyrimidine. Within a few minutes the hydrazone began to separate and after 10 minutes the reaction was apparently complete. The hydrazone is difficultly soluble in boiling alcohol, insoluble in water and soluble in dilute sodium hydroxide solution. It crystallizes in needles, which melt at about 295° to a dark oil. Analysis (Kjeldahl):

	Calculated for $C_{19}H_{18}ON_4S$	Found
N	16.00	15.95

Especially interesting was the behavior of phenylhydrazine towards 2-benzoylmethylmercapto-4-methyl-6-oxypyrimidine in glacial acetic acid solution. Five grams of the mercaptopyrimidine were dissolved in cold glacial acetic acid and 2.1 grams of phenylhydrazine added to the solution. There was no evidence of any reaction and the mixture was heated at 100° for about 2 hours. On cooling, a crystalline substance separated. This contained sulphur but did not melt below 300°. It was identified as 2-thio-4-methyluracil. Analysis (Kjeldahl);

	Calculated for $C_5H_6ON_2S$	Found
N	19.72	19.71

Reduction of the Hydrazone with Sodium Amalgam.—In this experiment 5 grams of the hydrazone and 15 grams of 3 per cent. amalgam were suspended in 75 cc. of alcohol and the reduction continued for about 12 hours at ordinary temperature. Eleven grams of amalgam were then added and the mixture allowed to stand for 12 hours. The greater part of the hydrazone had then dissolved and an insoluble gray prod-

uct was suspended in the alcohol. There was only a small amount of this, however, and it was not examined. After filtering, the red filtrate was acidified with hydrochloric acid, the sodium chloride separated by filtration and the solution then evaporated to dryness. We obtained a dark oily residue, which partially solidified after warming with water and cooling. The oil was extracted with ether and the aqueous solution evaporated, when we obtained, on cooling, 2-thio-4-methyluracil. Not enough material was dissolved by the ether for identification.

Reduction with Aluminium Amalgam.—In this experiment 4 grams of the hydrazone and an excess of amalgamated aluminium were suspended in a mixture of 300 cc. of alcohol and 50 cc. of water and this then warmed on the steam bath for 5 hours. Hydrogen sulphide was slowly evolved by this treatment. The mixture was finally filtered and the alcohol filtrate concentrated to a volume of about 10–15 cc., when 2-thio-4-methyluracil began to deposit in the form of needle-like prisms. On cooling, a small amount of oil also separated. No definite product was identified, however, except this thiopyrimidine. Analysis (Kjeldahl):

	Calculated for $C_5H_6ON_2S$	Found
N	19.72	19.70

Reduction of the Oxime of 2-Benzoylmethylmercapto-4-methyl-6-oxypyrimidine

With Sodium Amalgam.—Twelve and five-tenths grams of the oxime and an excess of amalgam (3 per cent.) were suspended in 100 cc. of 95 per cent. alcohol and the mixture then heated for one hour on the steam bath and allowed to stand for 10–12 hours at ordinary temperature. Ammonia was evolved during the heating. We obtained a yellow solution. This was acidified with hydrochloric acid, when a crystalline substance deposited mixed with sodium chloride. This solid was separated and purified by crystallization from hot water. It separated on cooling in slender prisms and was identified as 2-thio-4-methyluracil. Analysis (Kjeldahl):

	Calculated for $C_5H_6ON_2S$	Found
N	19.72	19.50

The alcohol filtrate (above) was evaporated to dryness, when more of the pyrimidine separated mixed with a basic oil. This mixture was then triturated with dilute sodium hydroxide to dissolve the pyrimidine and the oil extracted with ether and this finally dried over potash. After removal of the ether we obtained a dark red oil which we combined, without further attempts at purification, with phenyl isothiocyanate. They reacted immediately with evolution of heat, and a thick oil was obtained. After warming for a few minutes at 100° to complete the reaction the substance was then dissolved in a small volume of alcohol and the solution cooled. Prismatic crystals finally separated and melted after two crystallizations at 103°–105° to a clear oil. We did not obtain enough of this compound for analysis but it agreed in all its properties with the thiourea,

$$C_6H_5CH(CH_3).NH.CSNHC_6H_5$$[1]

With Ferrous Sulphate and Ammonia.—The oxime (3.5 grams) was dissolved in 100 cc. of dilute aqueous ammonia and combined with a solution of 35.5 grams of iron sulphate dissolved in 100 cc. of water. This mixture was then allowed to stand on the steam oven for about 24 hours, when the reduction was apparently complete. The iron oxide was then separated by filtration and the filtrate concentrated. The only products identified in this solution were ammonium sulphate and 2-thio-4-methyluracil. Therefore the oxime was reduced by ferrous sulphate in the same manner as by the amalgam.

With Formic Acid and Zinc Dust.—Eleven grams of the oxime were dissolved in 100 cc. of formic acid (specific gravity 1.12) and 10 grams of zinc dust added slowly to the solution. The temperature of the solution was not allowed to rise above 25°. Hydrogen sulphide was slowly evolved by this mild treatment. After allowing to stand for 2 days the acid was diluted with water and the zinc precipitated as zinc sulphide.

[1] Michaelis and Linow: Ber. d. chem. Ges., **26**, 2168.

After filtering off the zinc sulphide the filtrate was evaporated, when we obtained, as in the two preceding experiments, 2-thio-4-methyluracil.

NEW HAVEN, CONN.
July 1, 1912

A STUDY OF THE CONDUCTIVITY AND DISSOCIATION OF CERTAIN ORGANIC ACIDS AT 35°, 50° AND 65°

BY E. P. WIGHTMAN AND HARRY C. JONES

INTRODUCTION

[*This investigation was carried out with the aid of a Grant from the Carnegie Institution of Washington.*]

A fairly comprehensive study of the conductivity and dissociation of a large number of organic acids at temperatures from zero degrees to thirty-five degrees has already been made, and the results published in THIS JOURNAL.[1] In order to make this work as nearly complete as possible we have taken up the study of some of these same acids at fifty degrees and sixty-five degrees, repeating the work at thirty-five degrees.

It is not necessary to give a historical review of the literature of the subject, since this has already been done in connection with the work at lower temperatures. A summary of the conclusions previously arrived at is as follows:

1. "The temperature coefficients of conductivity, expressed in conductivity units, increase rapidly with dilution, and decrease rapidly with rise in temperature for weak organic acids—when not hydrated. When the acids are hydrated, the temperature coefficients of conductivity are larger, and their increase with dilution and decrease with rise in temperature both take place at a slower rate.

2. "Organic acids with the largest constants also have the largest temperature coefficients of conductivity expressed in conductivity units.

3. "The percentage temperature coefficients of conduc-

[1] White and Jones: THIS JOURNAL, **44**, 156 (1910). Wightman and Jones: *Ibid.*, **46**, 56 (1911).

tivity of the organic acids are generally small and of the same order of magnitude, and decrease with rise in temperature and with increase in dilution." The latter part of this statement, concerning the decrease of the percentage coefficients with increasing dilution, has been found to be incorrect and will be spoken of later.

4. "The conductivity of most of the organic acids is a parabolic function of the temperature, as proved by comparing observed values with those calculated from interpolation formulae.

5. "There is no general statement possible concerning the change in dissociation of the organic acids with change in temperature. Maxima occur with several between 25° and 35°, while in other cases maxima are indicated at slightly higher temperatures than those at which measurements were made. The dissociation of several acids decreases regularly from 0°.

6. "The strong organic acids do not obey the Ostwald dilution law, and, therefore, dissociation constants cannot be obtained for them in the ordinary way.

7. "The migration velocities of the anions of organic acids are a function of the number of atoms present in the anion, and μ_∞ values for dibasic acids may be found by means of this principle." More will be said of this farther on.

8. "Most dibasic organic acids dissociate like monobasic acids.

9. "Isomeric acids do not behave similarly as regards change in their dissociation.

10. "The migration velocities of isomeric ions are identical.

11. "The behavior of the organic acids with respect to the change in their dissociation with the temperature is not in accord with the hypothesis of Thomson and Nernst, which connects dissociating power and dielectric constants, or at least the influence of some other factor is suggested."

EXPERIMENTAL

The apparatus used in the present work was, in general, similar to that employed at lower temperatures.

The mother solutions of the acids were made up either in a 500 cc. or in a 250 cc. flask which had been calibrated for 50° in the following manner: The number of grams of water necessary to give 500 cc. of water at 50° was weighed into the flask and this calibrated at 20°. The 200 cc. flasks in which the other solutions were made up (from the mother solution) were all calibrated for 20° at 20°.

In making up a N/32 solution from an N/8 solution, the latter being the mother solution, 50 cc. of this was diluted to 200 cc. This 50 cc. of the original solution was of course too concentrated, but just enough so that when diluted in a 200 cc. flask calibrated at 20° for 20° it would give a solution which, when heated to 50°, would have the proper concentration, N/32.

The thermostats were similar to that used for 35° in the earlier work, except that the one for 50° and 65° was covered with an asbestos board impregnated with paraffin. There were two small holes for the thermometer and stirrer to pass through, and also holes large enough to place the cells in and take them out. Ordinarily these holes were covered with small pieces of asbestos board.

In this way the evaporation from the surface of the water in the thermostat was lessened, and the vapors above the surface were kept at a temperature not much lower than that of the bath itself. In consequence of this arrangement it was easier to keep the cells, both the exposed portion as well as the portion under water, at a more even temperature.

No account of the reagents used is necessary, since they were fully discussed in the previous paper.[1]

The procedure for obtaining the constants for the cells was as similar as possible to that for obtaining the conductivities of the acids. The cells, after having been previously kept at 50° for some time, were filled with the potassium chloride solution and then placed in the 25° bath. As soon as they had come to constant temperature, which usually required from about twenty minutes to a half hour, measure-

[1] This Journal, **48**, 62 (1911).

ments were made. A second series of readings was made a half hour later.

An important source of error, which must be taken into account in work at higher temperatures, is the solubility of the glass cell. West[1] and Clover[2], working with Jones, have both shown that this factor can be practically eliminated if certain precautions are taken. First, the cells must be thoroughly boiled out. Then they must be filled with pure water and be allowed to stand at a temperature somewhere about half way between the two extremes worked with; that is, about 50°. The cells were filled with fresh water every day, and, when not in use, were always kept at approximately this temperature. After about a week, no appreciable quantity of the glass will dissolve, provided the conditions are kept practically the same.

To test this, conductivity readings were made at 35°, then at 50° and 65°. The cells were then brought back to 35° and the conductivities measured again. It was found that the two 35° measurements agreed well with one another.

Keeping the cells always at an elevated temperature accomplished a twofold purpose; the first being that just mentioned, and, secondly, the expansion and contraction of the glass and platinum is not so great as to produce any appreciable effect on the cell constants and conductivity readings, as would probably be the case if there was any great change in temperature.

Sometimes on heating the cells to 50° and 60°, especially if they were allowed to stand at these higher temperatures for any length of time, a large number of gas bubbles would form on the electrodes. The cells were always shaken thoroughly in such cases, to get rid of the bubbles before making the measurements.

The cells were usually filled almost to the stoppers, since there was then little space left for evaporation and condensation, which might change the concentration of the solution quite appreciably.

[1] THIS JOURNAL, **34**, 508 (1905).
[2] *Ibid.*, **43**, 187 (1910).

RESULTS

The determination and use of the μ_∞ values of the sodium salts of the organic acids needs no explanation here.[1] The following table contains these values for 35°, 50° and 65°:

Table I.—μ_∞ Values for Sodium Salts

	35°	50°	65°
Cyanoacetic	105.8	135.6	171.9
Propionic	100.6	132.0	165.8
Levulinic	93.0	121.0	151.0
Hydroxyisobutyric	94.6	126.2	158.3
Isovaleric	95.5	123.0	153.8
Caprylic	95.4	119.4	159.9
Benzilic	88.6	135.6	171.9
o-Chlorobenzoic	93.5	123.0	153.5
o-Nitrobenzoic	95.2	123.8	155.5
m-Nitrobenzoic	95.2	124.4	156.3
p-Nitrobenzoic	95.2	123.0	153.8
1,2,4-Dinitrobenzoic	93.1	121.1	151.8
1,3,5-Dinitrobenzoic	93.3	121.7	152.6
m-Hydroxybenzoic	98.9	128.2	159.8
p-Hydroxybenzoic	98.9	127.4	158.9
1,2,4–Dihydroxybenzoic	95.2	122.6	153.4
p-Sulphamidobenzoic	93.6	123.3	154.4

A complete table of the μ_∞ values from 0° to 65° of all the acids worked with (except dichlorophthalic, tetrachlorophthalic and meconic acids) is as follows:

[1] THIS JOURNAL, **46**, 66 (1911).

Table II.—μ_∞ Values of the Acids

Acid	μ_∞ 0°	μ_∞ 15°	μ_∞ 25°	μ_∞ 35°	μ_∞ 50°	μ_∞ 65°
Trichloroacetic	224.8	303.9	355.9	406.4	478.5	520.9
Cyanoacetic	227.0	304.5	360.0	410.0	480.6	551.1
Propionic	223.0	...	354.0	405.0	477.0	545.0
Levulinic	220.9	298.2	348.3	396.9	466.0	430.2
Hydroxyisobutyric	222.8	304.1	357.5	407.4	471.2	537.5
Isovaleric	222.0	299.7	350.0	399.5	468.0	533.0
Caprylic	225.1	300.9	350.8	399.8	464.4	539.1
l-Tartaric	221.0	298.8	350.0	399.9	469.3	534.9
Thiodiglycolic	221.6	300.2	351.1	401.0	470.8	537.5
Tricarballylic	219.9	296.7	347.6	396.8	468.0	535.0
Benzilic	218.7	...	344.7	392.9	458.6	519.9
o-Nitrobenzoic	...	...	...	...	468.8	534.7
m-Nitrobenzoic	...	...	...	...	469.4	535.2
p-Nitrobenzoic	222.2	...	349.7	399.8	468.0	533.0
1,2,4-Dinitrobenzoic	220.0	297.3	347.9	396.8	466.1	531.0
1,3,5-Dinitrobenzoic	220.2	297.4	347.4	396.9	466.7	431.8
o-Chlorobenzoic	220.4	301.8	348.7	397.2	468.0	532.7
p-Hydroxybenzoic	223.0	...	353.0	403.0	472.4	538.1
m-Hydroxybenzoic	223.0	...	353.0	403.0	473.2	539.0
1,2,4-Dihydroxybenzoic	222.0	299.8	350.7	399.1	467.6	532.6
p-Sulphamidobenzoic	221.7	299.3	349.8	398.0	468.3	533.6
Benzenesulphonic	228.0	309.0	359.0	410.3	475.3	544.3
p-Toluenesulphonic	210.6	...	332.7	379.3	445.9	503.4
m-Nitrobenzenesulphonic	204.5	...	323.5	369.4	432.6	591.0
1,4,2-Nitrotoluenesulphonic	228.9	...	318.5	362.3	487.5	556.3
Camphoric	218.3	...	344.5	392.5	458.2	519.0

The μ_∞ values of the dibasic acids in the preceding table were found by means of the graphic method, previously described.[1] It can be seen, however, by glancing at the curve which is given below, that this means of determining the μ_∞ values is not as accurate at the higher temperatures as at the lower, because fewer of the values fall on a definite curve.

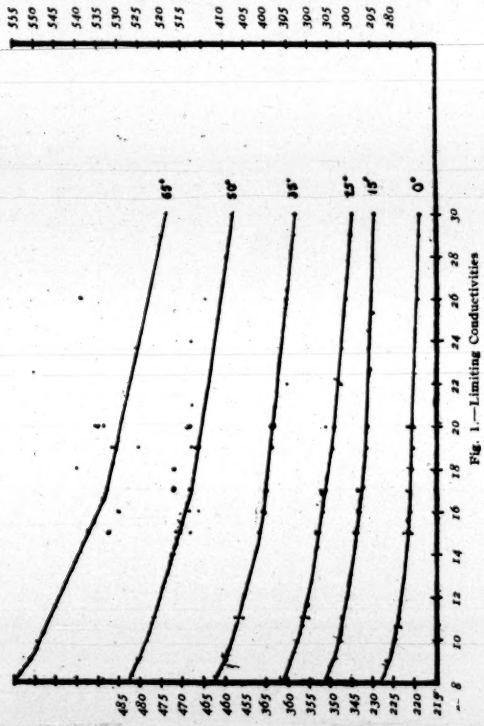


Fig. 1.—Limiting Conductivities

[1] Wightman and Jones: This Journal, 46, 69.

The values for the temperature coefficients between 35° and 50° in the following tables were calculated from the values for 35° in the previous paper in almost every case. The figures given for the percentage dissociation and dissociation constants are also taken from the earlier work. The agreement between the values for 35° in the present work and those given before was sufficiently close in most instances to justify this procedure. Where it was not, conductivity measurements were repeated, in which cases the later values were nearly always found to be correct, and so were used in the calculations.

The measurements of the conductivities of *o*-nitrobenzoic, *m*-nitrobenzoic, *m*-hydroxybenzoic and *p*-hydroxybenzoic acids were made by Dr. H. R. Kreider, formerly of this laboratory.

Trichloroacetic Acid

Table III.—Molecular Conductivity

V	35°	50°	65°
8	334.4	388.8	426.6
32	378.7	423.7	465.0
128	389.1	455.1	501.8
512	401.7	476.5	519.5
1024	406.3	478.5	520.9
2048	399.5	473.0	513.4

Table IV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	3.61	1.08	2.52	0.65
32	4.00	1.10	2.75	0.65
128	4.34	1.11	3.11	0.68
512	4.87	1.21	2.87	0.60
1024	4.80	1.18	2.83	0.59
2048	5.04	1.27	2.69	0.57

Table V.—Percentage Dissociation

V	35°	35°	65°
8	82.34	81.25	81.90
32	89.88	88.55	89.27
128	95.91	95.11	96.33
512	99.26	99.58	99.73
1024	100.00	100.00	100.00

Cyanacetic Acid

Table VI.—Molecular Conductivity

V	35°	50°	65°
8	66.31	74.70	80.43
32	118.8	134.0	144.5
128	199.6	227.8	249.0
512	292.7	337.3	368.0
1024	331.9	381.7	426.9
2048	358.4	418.1	472.6

Table VII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.57	0.87	0.38	0.51
32	1.01	0.85	0.70	0.52
128	1.87	0.93	1.41	0.62
512	2.95	1.01	2.05	0.60
1024	3.31	1.00	3.01	0.79
2048	4.10	1.15	3.63	0.87

Table VIII.—Percentage Dissociation

V	35°	50°	65°
8	16.53	15.55	14.59
32	28.97	27.88	26.22
128	48.70	47.40	45.18
512	71.46	70.18	66.78
1024	80.98	79.42	77.46
2048	86.97	86.99	85.75

Table IX.— Dissociation Constants $\times 10^4$

V	35°	50°	65°
8	39	36	31
32	37	34	29
128	36	33	29
512	35	32	26
1024	34	30	26
2048	28	27	25

Propionic Acid

Table X.—Molecular Conductivity

V	35°	50°	65°
2	1.925	2.195	2.444
8	4.198	4.740	5.231
32	8.415	9.59	10.39
128	16.54	18.88	20.29
512	32.13	36.30	39.23
1024	44.00	50.01	54.25
2048	59.66	67.00	73.66

Table XI.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
2	0.018	0.93	0.017	0.75
8	0.036	0.86	0.032	0.69
32	0.078	0.93	0.053	0.56
128	0.156	0.94	0.094	0.50
512	0.278	0.87	0.195	0.54
1024	0.401	0.91	0.283	0.57
2048	0.489	0.82	0.444	0.66

Table XII.—Percentage Dissociation

V	35°	50°	65°
2	0.47	0.46	0.45
8	1.04	0.99	0.96
32	2.08	2.01	1.91
128	4.07	3.96	3.72
512	7.93	7.61	7.20
1024	10.87	10.48	9.95
2048	14.88	14.04	13.51

Table XIII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
2	0.112	0.102	0.101
8	0.137	0.125	0.126
32	0.138	0.129	0.116
128	0.135	0.128	0.113
512	0.134	0.122	0.109
1024	0.130	0.120	0.108
2048	0.127	0.112	0.103

Levulinic Acid

Table XIV.—Molecular Conductivity

V	35°	50°	65°
8	5.636	6.463	7.189
32	11.13	12.96	14.39
128	21.90	25.54	28.38
512	41.78	48.08	51.79
1024	57.04	66.15	72.81
2048	75.98	86.98	95.76

Table XV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.062	1.12	0.048	0.75
32	0.124	1.12	0.095	0.74
128	0.247	1.15	0.189	0.74
512	0.43	1.03	0.247	0.51
1024	0.61	1.07	0.444	0.67
2048	0.70	0.91	0.585	0.67

Table XVI.—Percentage Dissociation

V	35°	50°	65°
8	1.40	1.39	1.36
32	2.80	2.78	2.71
128	5.50	5.48	5.35
512	10.50	10.32	9.77
1024	14.36	14.19	13.73
2048	19.28	18.66	18.06

Table XVII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
8	0.249	0.244	0.233
32	0.252	0.249	0.237
128	0.250	0.248	0.236
512	0.241	0.232	0.207
1024	0.235	0.229	0.213
2048	0.225	0.209	0.194

Hydroxyisobutyric Acid

Table XVIII.—Molecular Conductivity

V	35°	50°	65°
8	11.53	13.32	14.73
32	23.09	26.84	29.43
128	44.55	51.41	56.78
512	83.32	96.52	106.8
1024	111.5	128.3	141.8
2048	144.0	166.1	181.4

Table XIX.—Temperature Coefficients

	35°–65°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.12	1.00	0.094	0.71
32	0.26	1.13	0.173	0.65
128	0.45	1.01	0.36	0.70
512	0.88	1.06	0.68	0.71
1024	1.11	1.01	0.90	0.70
2048	1.47	1.02	1.02	0.61

Table XX.—Percentage Dissociation

V	35°	50°	65°
8	2.89	2.83	2.72
32	5.74	5.70	5.43
128	11.15	10.91	10.48
512	20.84	20.48	19.71
1024	27.88	27.23	26.17
2048	36.00	35.24	33.48

Table XXI.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
8	1.08	1.03	0.95
32	1.10	1.08	0.98
128	1.09	1.05	0.97
512	1.07	1.03	0.95
1024	1.08	1.00	0.91
2048	0.99	0.94	0.82

Isovaleric Acid

Table XXII.—Molecular Conductivity

V	0°	15°	25°
8	2.573	3.391	3.869
32	5.365	7.061	8.052
128	10.68	14.04	16.01
512	20.52	26.97	30.74
1024	28.28	37.11	42.18
2048	37.16	49.90	56.86

Table XXIII.—Temperature Coefficients

	0°–15°		15°–25°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.055	2.12	0.048	1.41
32	0.113	2.10	0.099	1.40
128	0.224	2.10	0.197	1.40
512	0.430	2.10	0.377	1.40
1024	0.589	2.08	0.507	1.37
2048	0.844	2.28	0.686	1.39

Table XXIV.—Percentage Dissociation

V	0°	15°	25°
8	1.16	1.13	1.11
32	2.42	2.36	2.30
128	4.81	4.69	4.57
512	9.24	9.00	8.78
1024	12.34	12.38	12.05
2048	16.74	16.65	16.25

Table XXV.—Dissociation Constants $\times 10^4$

V	0°	15°	25°
8	0.170	0.162	0.154
32	0.187	0.178	0.169
128	0.189	0.180	0.171
512	0.184	0.180	0.165
1024	0.170	0.171	0.161
2048	0.164	0.162	0.154

Table XXVI.—Molecular Conductivity

V	35°	50°	65°
8	4.392	4.877	5.115
32	8.927	9.89	10.57
128	17.68	19.52	20.94
512	33.71	36.95	39.92
1024	46.33	50.85	53.48
2048	62.55	69.79	72.93

Table XXVII.—Temperature Coefficients

	25°–35°		35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.	Cond. units	Per cent.
8	0.052	1.35	0.032	0.74	0.016	0.33
32	0.087	1.07	0.064	0.72	0.045	0.46
128	0.167	1.04	0.123	0.70	0.095	0.49
512	0.297	0.97	0.216	0.64	0.138	0.37
1024	0.415	0.98	0.301	0.65	0.175	0.34
2048	0.569	1.00	0.483	0.77	0.209	0.45

Table XXVIII.—Percentage Dissociation

V	35°	50°	65°
8	1.07	1.04	0.96
32	2.24	2.11	1.98
128	4.43	4.17	3.93
512	8.44	7.90	7.49
1024	11.60	10.87	10.03
2048	15.66	14.91	13.68

Table XXIX.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
8	0.145	0.137	0.116
32	0.160	0.143	0.125
128	0.160	0.142	0.126
512	0.152	0.132	0.119
1024	0.149	0.130	0.109
2048	0.140	0.128	0.101

Caprylic Acid

Table XXX.—Molecular Conductivity

V	35°	50°	65°
512	30.81	34.52	37.53
1024	42.37	47.28	50.57
2048	56.84	63.69	66.26

Table XXXI.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
512	0.23	0.74	0.201	0.58
1024	0.33	0.78	0.219	0.46
2048	0.45	0.80	0.170	....

Table XXXII.—Percentage Dissociation

V	35°	50°	65°
512	7.80	7.43	6.96
1024	10.64	10.18	9.38
2048	14.29	13.71	12.29

Table XXXIII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
512	0.129	0.117	0.102
1024	0.124	0.112	0.095
2048	0.116	0.106	0.084

Tartaric Acid

Table XXXIV.—Molecular Conductivity

V	35°	50°	65°
32	68.14	80.62	90.80
128	124.5	145.3	165.4
512	212.9	248.9	280.7
1024	263.1	308.4	348.9
2048	328.5	386.7	434.4

Table XXXV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	0.86	1.27	0.68	0.84
128	1.45	1.17	1.34	0.92
512	2.40	1.13	2.12	0.85
1024	3.12	1.19	2.70	0.88
2048	4.08	1.26	3.18	0.82

Table XXXVI.—Percentage Dissociation

V	35°	50°	65°
32	16.91	17.18	16.97
128	30.88	30.96	30.92
512	53.25	53.03	52.47
1024	65.40	65.71	65.23
2048	81.38	82.40	81.21

Table XXXVII.—Dissociation Constants × 10⁴

V	35°	50°	65°
32	10.8	11.1	11.1
128	10.8	10.8	10.8
512	11.8	11.7	11.3
1024	12.1	12.3	11.9
2048	17.4	18.8	17.1

Thiodiglycolic Acid

Table XXXVIII.—Molecular Conductivity

V	35°	50°	65°
8	28.54	32.50	35.68
32	52.64	60.64	66.48
128	96.25	111.0	122.5
512	168.5	194.9[1]	214.7
1024	216.0	249.8[1]	278.9
2048	275.3	318.0	355.3

Table XXXIX.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.29	1.03	0.212	0.65
32	0.57	1.09	0.389	0.64
128	1.00	1.04	0.767	0.69
512	1.67	0.99	1.32	0.68
1024	2.24	1.04	1.94	0.78
2048	2.82	1.03	2.49	0.78

Table XL.—Percentage Dissociation

V	35°	50°	65°
8	7.02	6.90	6.64
32	13.01	12.88	12.37
128	23.94	23.58	22.79
512	42.15	41.40	39.94
1024	53.90	53.06	51.88
2048	68.76	67.54	66.10

Table XLI.—Dissociation Constants × 10⁴

V	35°	50°	65°
8	6.63	6.39	5.90
32	6.08	5.95	5.46
128	5.89	5.68	5.26
512	6.00	5.71	5.19
1024	6.16	5.86	4.52
2048	7.39	6.86	6.29

[1] Interpolated values.

Tricarballylic Acid

Table XLII.—Molecular Conductivity

V	35°	50°	65°
8	16.28	19.29	22.09
32	32.33	37.97	42.97
128	62.39	73.72	82.46
512	115.0	135.7	150.2
1024	152.7	180.2	203.1
2048	196.5	230.8	261.6

Table XLIII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	0.20	1.23	0.187	0.97
32	0.35	1.08	0.333	0.88
128	0.76	1.22	0.583	0.79
512	1.35	1.17	0.97	0.71
1024	1.85	1.21	1.22	0.68
2048	2.28	1.16	2.05	0.89

Table XLIV.—Percentage Dissociation

V	35°	50°	65°
8	4.09	4.12	4.13
32	8.16	8.11	8.03
128	15.09	15.75	15.41
512	29.06	29.00	28.07
1024	38.39	38.50	37.96
2048	49.54	49.31	48.90

Table XLV.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
8	2.18	2.21	2.22
32	2.27	2.24	2.19
128	2.28	2.30	2.19
512	2.33	2.31	2.14
1024	2.34	2.35	2.27
2048	2.38	2.30	2.28

Benzilic Acid

Table XLVI.—Molecular Conductivity

V	35°	50°	65°
128	114.3	...	...
512	192.4	220.6	240.4
1024	237.1	266.5	293.0
2048	281.4	320.8	348.5

Table XLVIII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
128	....	....	....	....
512	1.88	0.98	1.29	0.58
1024	1.96	0.83	1.77	0.66
2048	2.63	0.93	1.85	0.58

Table XLIX.—Percentage Dissociation

V	35°	50°	65°
128	29.97	...	...
512	47.57	48.01	46.24
1024	60.20	58.11	56.36
2048	64.82	69.95	67.03

Table L.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
128	9.46	....	....
512	8.43	8.66	7.77
1024	8.89	7.87	7.09
2048	5.83	7.95	6.65

Meconic Acid

Table LI.—Molecular Conductivity

V	35°	50°	65°
32	461.5	524.4	574.2
128	599.0	684.7	754.9
512	728.9	839.2	940.8
1024	778.3	899.0	1027.8
2048	803.2	945.0	1081.2

Table LII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	4.19	0.91	3.32	0.63
128	5.72	0.94	4.68	0.68
512	7.31	1.00	6.77	0.80
1024	8.07	1.04	8.59	0.96
2048	9.49	1.18	9.08	0.96

o-*Chlorobenzoic Acid*

Table LIII.—Molecular Conductivity

V	35°	50°	65°
128	128.6	138.4	143.1
256	168.7	182.3	189.3
512	211.8	231.8	240.1
1024	256.3	281.9	298.8
2048	294.7	329.2	350.5

Table LIV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
128	0.67	0.52	0.313	0.23
256	1.01	0.60	0.467	0.26
512	1.33	0.63	0.553	0.24
1024	1.70	0.66	1.13	0.40
2048	2.15	0.73	1.42	0.43

Table LV.—Percentage Dissociation

V	35°	50°	65°
128	32.32	29.56	28.70
256	42.06	38.95	37.97
512	53.33	49.53	48.16
1024	64.53	60.23	49.94
2048	74.74	70.34	70.31

Table LVI.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
128	12.1	0.97	0.90
256	11.9	0.97	0.91
512	11.9	0.95	0.87
1024	11.5	0.89	0.88
2048	10.8	0.82	0.82

o-*Nitrobenzoic Acid*[1]

Table LVII.—Molecular Conductivity

V	35°	50°	65°
32	138.0	144.9	147.2
128	223.6	240.8	249.9
512	308.7	345.9	370.6
1024	347.8	393.5	426.8
2048	369.8	425.9	474.4

[1] Measurements made by Dr. H. R. Kreider.

Table LVIII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	0.29	0.20	0.15	0.11
128	1.21	0.54	0.61	0.25
512	2.54	0.83	1.65	0.48
1024	3.77	1.12	2.22	0.55
2048	4.94	1.40	3.23	0.75

Table LIX.—Percentage Dissociation

V	35°	50°	65°
32	35.2	30.91	27.53
128	55.7	51.36	46.74
512	77.0	73.78	69.31
1024	84.2	83.94	79.82
2048	88.0	90.86	88.72

Table LX.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
32	59.7	43.2	32.7
128	54.7	42.4	32.1
512	50.3	32.2	30.6
1024	43.7	42.8	30.8
2048	34.4	55.2	34.1

m-*Nitrobenzoic Acid*[1]

Table LXI.—Molecular Conductivity

V	35°	50°	65°
128	77.56	89.9	99.9
512	137.1	160.1	177.9
1024	175.4	210.7	235.9
2048	216.7	262.9	295.7

Table LXII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
128	0.82	1.06	0.67	0.74
512	1.53	1.12	1.19	0.74
1024	2.35	1.34	1.67	0.78
2048	3.08	1.42	2.19	0.83

[1] Measurements made by Dr. H. R. Kreider.

Table LXIII.—Percentage Dissociation

V	35°	50°	65°
128	19.2	19.1	18.7
512	33.9	34.1	33.2
1024	43.4	44.9	44.0
2048	53.6	56.0	55.2

Table LXIV.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
128	3.57	3.54	3.34
512	3.40	3.44	3.32
1024	3.25	3.57	3.38
2048	3.02	3.48	3.33

p-*Nitrobenzoic Acid*

Table LXV.—Molecular Conductivity

V	35°	50°	65°
512	147.7	170.6	187.9
1024	189.9	218.7	238.6
2048	235.0	275.2	304.2

Table LXVI.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
512	1.49	1.00	1.15	0.67
1024	2.09	1.12	1.33	0.61
2048	2.65	1.13	1.93	0.70

Table LXVII.—Percentage Dissociation

V	35°	50°	65°
512	37.12	36.45	35.18
1024	46.86	46.73	44.76
2048	58.87	58.80	57.07

Table LXVIII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
512	4.28	4.08	3.52
1024	4.03	4.00	3.54
2048	4.11	4.09	3.70

1,2,4-Dinitrobenzoic Acid

Table LXIX.—Molecular Conductivity

V	35°	50°	65°
32	259.4	284.5	301.6
128	333.8	376.2	412.0
512	381.2	443.4	493.2
1024	391.5	459.8	512.6
2048	398.1	466.7	525.4

Table LXX.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	1.53	0.63	1.14	0.40
128	2.66	0.79	2.39	0.64
512	4.30	1.14	3.32	0.75
1024	4.59	1.17	3.52	0.77
2048	4.66	1.17	3.91	0.84

Table LXXI.—Percentage Dissociation

V	35°	50°	65°
32	65.49	61.04	57.40
28	84.74	80.71	78.42
512	95.47	95.13	93.87
1024	98.49	98.65	97.56
2048	100.00	100.00	100.00

1,3,5-Dinitrobenzoic Acid

Table LXXII.—Molecular Conductivity

V	35°	50°	65°
512	335.6	279.7	311.8
1024	280.9	328.7	366.0
2048	324.5	382.1	426.9

Table LXXIII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
512	3.08	1.32	2.14	0.77
1024	3.25	1.16	2.49	0.76
2048	3.84	1.19	3.16	0.74

Table LXXIV.—Percentage Dissociation

V	35°	50°	65°
512	58.83	59.93	59.35
1024	70.54	70.43	69.66
2048	78.86	81.31	81.25

Table LXXV.—Dissociation Constants × 10⁴

V	35°	50°	65°
512	16.4	17.5	16.4
1024	16.5	16.4	15.6
2048	14.4	17.3	17.2

m-*Hydroxybenzoic Acid*[1]

Table LXXVI.—Molecular Conductivity

V	35°	50°	65°
64	27.74	31.74	34.75
128	38.63	44.46	48.77
512	73.28	83.92	92.10
1024	99.70	116.0	127.5
2048	132.6	151.9	167.6

Table LXXVII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
64	0.27	0.98	0.20	0.64
182	0.39	1.01	0.29	0.64
512	0.71	0.97	0.54	0.64
1024	1.09	1.09	0.77	0.66
2048	1.29	0.99	1.04	0.68

Table LXXVIII.—Percentage Dissociation

V	35°	50°	65°
64	6.88	6.7	6.4
128	9.58	9.4	9.1
512	18.19	17.7	17.1
1024	24.74	24.5	23.6
2048	32.91	32.1	31.1

Table LXXIX.—Dissociation Constants × 10⁴

V	35°	50°	65°
64	0.795	0.755	0.694
128	0.794	0.764	0.689
512	0.798	0.745	0.687
1024	0.794	0.752	0.692
2048	0.788	0.743	0.685

Measurements made by Dr. H. R. Kreider.

p-*Hydroxybenzoic Acid*[1]

Table LXXX.—Molecular Conductivity

V	35°	50°	65°
65	16.94	19.41	21.43
128	23.38	26.70	29.38
512	45.33	51.95	57.15
1024	63.66	72.92	80.22
2048	86.67	99.51	109.38

Table LXXXI.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
64	0.16	0.94	0.13	0.69
128	0.20	0.84	0.27	0.67
512	0.41	0.90	0.35	0.68
1024	0.65	1.00	0.49	0.67
2048	0.93	1.01	0.66	0.67

Table LXXXII.—Percentage Dissociation

V	35°	50°	65°
64	4.21	4.11	3.98
128	5.88	5.65	5.46
512	11.36	11.00	10.62
1024	15.70	15.43	14.91
2048	21.00	21.07	20.33

Table LXXXIII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
64	0.289	0.275	0.258
128	0.287	0.267	0.246
512	0.284	0.239	0.245
1024	0.285	0.275	0.261
2048	0.273	0.275	0.253

1,2,4-Dihydroxybenzoic Acid

Table LXXXIV.—Molecular Conductivity

V	35°	50°	65°
128	92.25	109.2	122.2
512	160.3	189.7	211.9
1024	205.6	241.4	266.7
2048	253.6	294.4	322.1

[1] Measurements made by Dr. H. R. Kreider.

Table LXXXV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
128	1.14	1.24	0.863	0.79
512	1.85	1.14	1.48	0.78
1024	2.52	1.24	1.69	0.70
2048	3.08	1.24	1.85	0.63

Table LXXXVI.—Percentage Dissociation

V	35°	50°	65°
128	23.10	23.35	22.94
512	40.62	40.48	39.78
1024	51.04	51.63	50.07
2048	62.24	62.96	60.48

Table LXXXVII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
128	5.42	5.06	5.33
512	5.43	5.38	5.13
1024	5.12	5.38	4.90
2048	5.01	5.23	4.52

m-*Aminobenzoic Acid*[1]

Table LXXXVIII.—Molecular Conductivity

V	0°	18°	25°	35°
128	3.57	6.91	8.54	11.09
512	6.16	10.33	12.17	14.96
1024	11.75	22.61	27.77	35.57
2048	17.20	32.38	39.37	50.01

Table LXXXIX.—Temperature Coefficients

	0°–18°		18°–25°		25°–35°	
V	Cond. units	Per cent.	Cond. units	Per cent.	Cond. units	Per cent.
128	0.19	5.3	0.23	3.3	0.25	2.9
512	0.23	3.7	0.25	2.4	0.28	2.3
1024	0.60	5.3	0.74	3.3	0.78	2.5
2048	0.84	4.9	1.00	3.0	1.06	2.7

Table XC.—Percentage Dissociation

V	0°	18°	25°	35°
128	1.69	2.26	2.57	2.82
512	2.97	3.38	3.66	3.80
1024	5.57	7.39	8.35	9.04
2048	8.15	10.59	11.83	12.71

[1] The Ostwald dilution law would not give dissociation constants for this acid.

p-*Sulphamidobenzoic Acid*

Table XCI.—Molecular Conductivity

V	35°	50°	65°
512	127.9	148.3	163.5
1024	167.3	189.1	213.1
2048	209.6	243.9	270.5

Table XCII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
512	1.35	1.06	1.01	0.68
1024	1.45	0.87	1.27	0.67
2048	2.26	1.08	1.77	0.75

Table XCII.—Percentage Dissociation

V	35°	50°	65°
512	32.17	31.67	30.64
1024	42.01	40.38	39.93
2048	52.79	52.08	50.69

Table XCIII.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
512	2.98	2.87	2.64
1024	2.97	2.67	2.59
2048	2.88	2.76	2.54

Benzenesulphonic Acid

Table XCIV.—Molecular Conductivity

V	35°	50°	65°
8	366.1	429.3	484.9
32	370.1	453.0	515.4
128	399.8	473.9	540.6
512	407.0	475.3	544.3
1024	410.3	474.2	544.2
2048	407.1	472.9	540.1

Table XCV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	4.21	1.15	3.71	0.86
32	5.53	1.49	4.16	0.92
128	4.94	1.23	4.45	0.94
512	4.55	1.12	4.60	0.97
1024	4.26	1.04	4.67	0.98
2048	4.39	1.08	4.48	0.95

Table XCVI.—Percentage Dissociation

V	35°	50°	65°
8	89.23	90.32	89.09
32	90.20	95.30	94.69
128	97.44	99.70	99.30
512	99.20	100.00	100.00
1024	100.00	100.00	100.00

m-*Nitrobenzenesulphonic Acid*

Table XCVII.—Molecular Conductivity

V	35°	50°	65°
32	347.2	409.0	465.5
128	357.3	419.5	478.4
512	366.8	430.4[1]	489.5
1024	367.9	432.6	491.0
2048	366.5	...	...

Table XCVIII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	3.93	1.12	3.77	0.92
128	4.15	1.16	3.93	0.94
512	4.24	1.15	3.94	0.92
1024	4.21	1.14	3.89	0.90

Table XCIX.—Percentage Dissociation

V	35°	50°	65°
32	94.75	94.54	94.80
128	96.69	96.97	97.43
512	99.40	99.49	99.69
1024	100.00	100.00	100.00

p-*Toluenesulphonic Acid*

Table C.—Molecular Conductivity

V	35°	50°	65
32	363.2	430.3	489.4
128	374.7	440.0	499.3
512	376.8	444.2	502.0
1024	380.3	445.9	503.4
2048	379.8	445.3	502.6

[1] Interpolated value.

Table CI.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
32	4.59	1.27	3.94	0.92
128	4.39	1.17	3.95	0.90
512	4.52	1.20	3.85	0.87
1024	4.44	1.17	3.83	0.86
2048	4.89	1.31	3.82	0.86

Table CII.—Percentage Dissociation

V	35°	50°	65°
32	95.30	96.50	97.20
128	98.68	98.67	99.19
512	99.26	99.61	99.72
1024	100.00	100.00	100.00

1,4,2-Nitrotoluenesulphonic Acid

Table CIII.—Molecular Conductivity

V	0°	16°	25°
8	203.0	281.8	320.5
32	221.6	308.7	349.5
128	225.3	312.8	355.6
512	228.3	317.5	360.7
1024	228.9	318.5	362.3
2048	228.0	318.7	360.8

Table CIV.—Temperature Coefficients

	0°–16°		16°–25°		25°–35°	
V	Cond. units	Per cent.	Cond. units	Per cent.	Cond. units	Per cent.
8	4.90	2.41	4.30	1.53	4.38	1.37
32	5.42	2.44	4.53	1.47	4.36	1.25
128	5.44	2.41	4.76	1.52	5.20	1.46
512	5.55	2.43	4.80	1.51	5.11	1.42
1024	5.58	2.44	4.87	1.53	4.95	1.37
2048	5.65	2.48	4.68	1.47	5.14	1.42

Table CV.—Percentage Dissociation

V	0°	16°	25°
8	88.68	88.48	88.46
32	96.81	96.92	96.47
128	98.43	98.21	98.15
512	99.74	99.69	99.56
1024	100.00	100.00	100.00

1,4,2-Nitrotoluenesulphonic Acid

Table CVI.—Molecular Conductivity

V	35°	50°	65°
8	364.3	433.3	493.4
32	393.1	462.1[1]	524.8
128	407.6	476.7	542.6
512	411.8	486.0	554.5
1024	413.6	487.5	556.3
2048	412.2	485.4	553.2

Table CVII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
8	4.60	1.26	4.01	0.92
32	4.60	1.17	4.18	0.91
128	4.61	1.13	4.39	0.92
512	4.95	1.20	4.57	0.94
1024	4.92	1.19	4.59	0.94
2048	4.88	1.18	4.52	0.93

Table CVIII.—Percentage Dissociation

V	35°	50°	65°
8	88.08	88.88	88.69
32	95.04	94.79	94.34
128	98.55	97.78	97.54
512	99.56	99.69	99.67
1024	100.00	100.00	100.00

Dichlorophthalic Acid

Table CIX.—Molecular Conductivity

V	35°	50°	65°
128	318.9	354.7	378.7
512	397.5	451.7	492.5
1024	441.6	499.3	543.3
2048	493.0	562.8	614.0

Table CX.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
128	2.42	0.76	1.60	0.45
512	3.55	0.89	2.72	0.60
1024	3.91	0.89	2.93	0.59
2048	5.02	1.03	3.41	0.60

[1] Interpolated value.

Tetrachlorophthalic Acid

Table CXI.—Molecular Conductivity

V	35°	50°	65°
512	492.6	552.7	601.3
1024	555.2	617.4	669.3
2048	605.5	684.9	739.6

Table CXII.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units	Per cent.
512	4.00	0.81	3.24	0.59
1024	4.15	0.75	3.46	0.56
2048	5.33	0.88	3.65	0.53

Camphoric Acid

Table CXIII.—Molecular Conductivity

V	35°	50°	65°
512	42.27	47.53	51.30
1024	57.54	63.86	69.26
2048	76.74	86.20	93.84

Table CXIV.—Temperature Coefficients

	35°–50°		50°–65°	
V	Cond. units	Per cent.	Cond. units.	Per cent.
512	0.33	0.78	0.258	0.54
1024	0.39	0.67	0.360	0.56
2048	0.69	0.91	0.509	0.59

Table CXV.—Percentage Dissociation

V	35°	50°	65°
512	10.85	10.37	9.88
1024	14.78	13.94	13.34
2048	19.40	18.81	18.08

Table CXVI.—Dissociation Constants $\times 10^4$

V	35°	50°	65°
512	0.259	0.234	0.212
1024	0.250	0.220	0.201
2048	0.228	0.213	0.195

Discussion

It can be readily seen from the figures given above for the temperature coefficients that the statement in the introduc-

tion concerning them at lower temperature holds good up to 65°. It should be noted, however, that the temperature coefficients in per cent. have become at 65°—except with the strong acids—almost negligible.

The statement was made previously that these coefficients usually decrease with increase in dilution. A more careful study shows that no such general statement can be made. A large number increase, and some are quite irregular. The increase in the case of *o*- and *m*-nitrobenzoic acids, and one or two others, is especially worthy of mention. The variation amounts to fifty per cent. or more between the most concentrated and the most dilute solutions.

Whatever the reasons for the irregularity in connection with the temperature coefficients expressed in per cent., the fact that there is no general uniformity indicates a complicated state of affairs. We usually speak of conductivity being determined by the number and velocity of the ions—the number depending upon the amount of dissociation, which, in turn, is a function of the association of the solvent, the concentration, and the temperature, and perhaps of other causes of which we are not yet fully aware; the velocity being a function of the viscosity of the solution, the ionic volume and the specific character of the ion. Owing to the close interrelationship of these various factors, which may all be varying at once, it is almost impossible to predict the result of combining them.

The work at higher temperatures shows that the statement made in the previous work concerning the change in dissociation of the organic acids with change in temperature is correct, so far as it goes. A more general statement, however, can now be made. Whatever the change in dissociation at lower temperatures—with some acids there is a constant decrease from 0°, with others a maximum value at some intermediate temperature—there is in every case a decrease in the dissociation in passing from fifty degrees to any higher temperature.

Mention has already been made of the fact that the μ_∞ values for the dibasic acids are not as readily obtained at 50° and 65° as at the lower temperatures, on account of fewer of

the values for μ_∞ falling on a definite curve when plotted against the number of atoms in the anion.

Since the μ_∞ values for several of the strong acids, and some others, even at lower temperatures, do not fit into this curve, it is safe to say that there is some other factor in addition to the mere number of atoms in the anion which likewise affects the magnitude of the μ_∞ value. Perhaps their arrangement has some influence, but more likely the amount of hydration which, of course, changes the size and mass of the anion, and which has not been taken into account in this work, plays a very important part.

Rise in temperature does not produce exactly the same effect on every hydrated substance, and we would expect a greater variation in the effect produced at higher than at lower temperatures. It might be claimed that the acids are not sufficiently hydrated to be thus affected. Not so with the sodium salts of the acids, however, and it is by means of them that the μ_∞ values are obtained for the monobasic acids.

All other conclusions reached heretofore have been confirmed in the present work, and as they have already been summarized in the introduction to the present paper further mention of them is not necessary.

SUMMARY

No conclusion, in explanation of the irregularities in the percentage temperature coefficients, could be arrived at, except that they are the result of a large number of varying factors which are closely interrelated.

Higher temperature causes a decrease in dissociation.

The values of μ_∞ for the organic acids, plotted against the number of atoms in the anion, do not give a very even curve. The cause for this probably lies in the fact that the sodium salts, from the μ_∞ values of which the μ_∞ values of the acids are obtained, are more or less hydrated and the rising temperature produces varying effects

Work is now in progress on a much larger number of

organic acids, and these substances will also be studied in nonaqueous and mixed solvents.

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BALTIMORE, MD.
May, 1912

ON THE MECHANISM OF ORGANIC REACTIONS

BY S. F. ACREE

[TWELFTH COMMUNICATION ON CATALYSIS]

(We have been aided in these researches by the Carnegie Institution of Washington.)

ALKALINE CATALYSIS

As a further contribution to our theory that in all reactions we should consider the possibility of the direct transformation of both ions and nonionized[1] substances the writer presents[2] work by Dr. H. C. Robertson, Dr. E. K. Marshall, Dr. Julia Peachy Harrison, Miss B. Marion Brown, Dr. J. Chandler, Dr. Sidney Nirdlinger, Dr. F. M. Rogers, Dr. C. N. Myers and Mr. J. H. Shrader on the reactions of alkyl halides with sodium, potassium and lithium ethylates, with sodium, potassium and lithium phenolates, and with sodium phenylthiourazole, and on the reversible addition of ethyl alcohol to nitriles when catalyzed by ethylates, in absolute ethyl alcohol. We are showing, furthermore, how the theory is aided by the work of Stieglitz, of Goldschmidt and of Tubandt. The experimental and mathematical details of our researches will appear soon as publications in THIS JOURNAL and as a monograph of the Carnegie Institution of Washington.

If the ethylate ion reacts with the molecular alkyl halide and forms the halide ion and an ether, and the nonionized sodium ethylate also reacts with the molecular alkyl halide

[1] THIS JOURNAL, **27**, 118; **28**, 370; **31**, 185; **32**, 606; **37**, 71, 361; **38**, 1, 258, 489, 746; **39**, 124, 145, 226, 300; **41**, 457, 483; **42**, 115; **43**, 358, 505; **44**, 219. Ber. d. chem. Ges., **33**, 1520; **35**, 553; **36**, 3139; **37**, 184, 618; **41**, 3199. Science, **30**, 617 (1909). J. Am. Chem. Soc., **30**, 1755.

[2] A short article on this subject was presented at the New York meeting of the Int. Congress of Applied Chem., September, 1912.

and yields the sodium halide and the ether, the reaction can be represented as follows:

$$C_2H_5I + \bar{O}C_2H_5 \longrightarrow (C_2H_5)_2O + \bar{I}$$

$$C_2H_5I + \left\{ \begin{matrix} NaOC_2H_5 \text{ or} \\ + \quad - \\ Na + \bar{O}C_2H_5 \end{matrix} \right\} \longrightarrow (C_2H_5)_2O + NaI, \text{ or}$$

$$\begin{aligned} \frac{dx}{dt} &= K_i\alpha(C_{salt} - x)(C_{alkyl\ halide} - x) \\ &+ K_m(1 - \alpha)(C_{salt} - x)(C_{alkyl\ halide} - x) \\ &= [K_i\alpha + K_m(1 - \alpha)](C_{salt} - x)(C_{alkyl\ halide} - x) \\ &= K_V(C_{salt} - x)(C_{alkyl\ halide} - x) \end{aligned}$$

K_i (see note, p. 378) is the reaction velocity of the alkyl halide and the ethylate (phenolate, urazole, etc.) anion, K_m is the reaction velocity of the alkyl halide and the nonionized sodium ethylate (potassium ethylate, etc.), α is the per cent. of ionization of the sodium ethylate as determined by the conductivity method by Dr. H. C. Robertson, C_{salt} is the initial concentration of the sodium ethylate, i. e., one gram molecule in V liters, $C_{alkyl\ halide}$ is the initial concentration of the alkyl halide, and x is the change in the concentration of the sodium ethylate and of the alkyl halide in the time t.

On integration we get the equations

$$K_V = K_i\alpha + K_m(1 - \alpha) = \frac{x}{t(A - x)} \text{ or}$$

$$\frac{B}{t(A - B)} \log_n \frac{B(A - x)}{A(B - x)}$$

When the values of K_V are multiplied by V we secure the expressions

$$\begin{aligned} VK_V &= K_n = K_i\alpha + K_m(1 - \alpha) \\ V'K_{V'} &= K'_n = K_i\alpha' + K_m(1 - \alpha') \\ V''K_{V''} &= K''_n = K_i\alpha'' + K_m(1 - \alpha'') \end{aligned}$$

which give us the reaction velocity, K_n, K'_n or K''_n, which the solution would have if the concentration of the sodium ethylate were unity and the ionization were α, α' or α''. When these

equations are solved simultaneously we secure the unknown values of K_i and K_m from the expressions

$$K_i = \frac{K'_n(1-\alpha) - K_n(1-\alpha')}{\alpha' - \alpha}$$

and

$$K_m = \frac{K_n\alpha' - K'_n\alpha}{\alpha' - \alpha}.$$

The various values of K_i and K_m so obtained should be, and are, constant within the experimental errors, whatever the value of V. Since we have measured the ionization and reaction velocities of the ethylates in solutions varying from N/1 to N/32 there is a wide variation in K_V and α; but the values of K_i and K_m for sodium ethylate and methyl iodide are found by Dr. Robertson to be quite constant and to give the average $K_i = 0.127$ and $K_m = 0.0594$ (see Table III below). These results make plausible our interpretation that both the ethylate ions and the nonionized sodium ethylate react with the alkyl halides.

In the following tables are given as briefly as possible, as an example, some of the experimental results which Dr. H. C. Robertson has obtained for a typical case, the reaction of sodium ethylate with methyl iodide at 25°. In Table I are given the values of α and $(1-\alpha)$ corresponding to the different values of V. Each value of K_n in Table II is the mean of a large number obtained when the reactions were allowed to take place during different intervals of time. The values of K_i and K_m with asterisks in Table III are those in which there are smaller experimental errors involved in $\alpha'-\alpha$ and other factors. As is generally the case, the average of these values with least errors is practically the same as the average of all the values obtained. In Table IV we give a comparison of K_n "found" and K_n "calculated" from the values of K_i and K_m; the magnitude of the experimental errors is thus clearly shown. Naturally all of these results are subject to the slight revision which must always accompany a more careful repetition of any investigation.

Table I.—Ionization of Sodium Ethylate at 25°

V	α	$(1-\alpha)$
1	0.148	0.852
2	0.234	0.766
4	0.312	0.688
8	0.393	0.607
16	0.481	0.519
40	0.605	0.395

Table II.—Values of K_n for Sodium Ethylate and Methyl Iodide at 25°

V	K_n	K_n (average)
2	0.0748	0.0750
	0.0752	
4	0.0812	0.0808
	0.0804	
8	0.0856	0.0857
	0.0858	
16	0.0923	0.0923
	0.0923	
40	0.1020	0.0998
	0.0976	

Table III.—K_i and K_m for Sodium Ethylate and Methyl Iodide at 25°

V	K_i	K_m
$V=2$: $V=4$	0.132	0.0577
$V=2$: $V=8$	0.127*	0.0591*
$V=2$: $V=16$	0.129*	0.0586*
$V=2$: $V=40$	0.126*	0.0593*
$V=4$: $V=8$	0.123	0.0616
$V=4$: $V=16$	0.127*	0.0595*
$V=4$: $V=40$	0.125*	0.0605*
$V=8$: $V=16$	0.130	0.0567
$V=8$: $V=40$	0.126*	0.0597*
$V=16$: $V=40$	*0.124*	*0.0632*
Average	0.127	0.0596
Average[1]	0.127	0.0594

[1] The average of all values with asterisks involves smaller errors.

Table IV.—K_n "Found" and K_n "Calculated" for Sodium Ethylate and Methyl Iodide at 25°

V	K_n found	K_n calculated (1) $\{K_i = 0.1270, K_m = 0.0596$	(2) $\{K_i = 0.1270, K_m = 0.0594$	Error in per cent. (1)	Error in per cent. (2)
2	0.0750	0.0753	0.0752	—0.4	—0.3
4	0.0808	0.0807	0.0805	+0.1	+0.4
8	0.0857	0.0861	0.0860	—0.5	—0.4
16	0.0923	0.0920	0.0919	+0.3	+0.5
40	0.0998	0.1004	0.1002	—0.6	—0.4

But if this theory is correct we should obtain the same value for K_i *for the ethylate ion* when we study the reaction of methyl iodide with sodium ethylate and with potassium ethylate, although the values of K_m may differ in the two reactions. Still more conclusive evidence for the theory, therefore, is the fact that Dr. Julia P. Harrison finds that potassium ethylate and methyl iodide, in solutions varying from 0.25 N to 0.03125 N, give the same average value, $K_i = 0.127$, for the ethylate ion that Dr. Robertson obtains from sodium ethylate and methyl iodide. This is especially striking in view of the fact that the molecular potassium ethylate, for which $K_m = 0.066$ for this reaction, reacts 12 per cent. faster with the methyl iodide than does the molecular sodium ethylate.

Another line of evidence for our theory is the fact that in *dilute solutions* the addition of sodium iodide to sodium ethylate and methyl iodide, for example, suppresses the ionization of the sodium ethylate, and therefore its reaction velocity, to exactly the extent that we calculate from the Arrhenius theory of isohydric solutions and from our theory of the mechanism of this class of reactions. When several equivalents of sodium iodide are added to one of sodium ethylate (N/32) the reaction velocity is slightly smaller than the theoretical value. Dr. H. C. Robertson has shown experimentally that the Arrhenius theory of isohydric solutions applies closely in all of our work. When an added salt changes the reaction velocity exactly as demanded by our theory we consider the "salt effect" to be "normal." When the concentration of

the added salt becomes so large that the reaction velocity does not correspond exactly to the calculated value, we call this deviation a positive or negative[1] "abnormal salt effect." We believe that an "abnormal salt effect" is due to a change in the physical conditions of the solution, or to the formation of *new double compounds* which are more or less reactive than the constituent parts, either of which causes will be most evident in the concentrated solutions. We are studying the question whether the ionic and molecular reactions are affected alike by the ions and nonionized salts.

Still other satisfactory evidence for the theory is the fact that Dr. H. C. Robertson and Mr. J. H. Shrader have shown that sodium phenolate, potassium phenolate and lithium phenolate have different degrees of ionization in the same concentrations and react with different velocities with methyl iodide, and yet these three salts, in concentrations varying from N to 0.03125 N, give the same value for K_i, namely 0.0282, 0.0283 and 0.0284, respectively. The values of K_m are 0.00474, 0.0037 and 0.0040, respectively, this wide variation harmonizing very nicely with our theory because of the differences in the nonionized sodium, potassium and lithium phenolates. Added sodium iodide produces a positive "abnormal salt effect."

Dr. J. Chandler proved, as did also Dr. Sidney Nirdlinger and Dr. F. M. Rogers working together,[2] that ethyl iodide reacts with both the anion and the nonionized portion of the cyclic amide[3] sodium phenylthiourazole in ethyl alcohol at

[1] For the equations covering such cases see Acree and coworkers: Ber. d. chem. Ges., **41**, 3208. e. g., $[1+(f)\ C_{salt}][K_i\alpha+K_m(1-\alpha)](C_{salt}-x)(C_{alkyl\ halide}-x)$.

[2] This work was finished in May, 1908, and reported in THIS JOURNAL, **43**, 519, 551. Although recognizing the possibility of the reaction of the nonionized salt, we interpreted the first crude data of Shadinger, Brunel and Johnson as reactions "chiefly" of the urazole anions (THIS JOURNAL, **39**, 228–236). In THIS JOURNAL, **38**, 261, we wrote: "If the other urazole groups are concerned in the reaction it is to only a minor extent." The final work now shows the nonionized salt to be more reactive than we then believed.

[3] It is possible that in the Hofmann and Lossen rearrangements both tautomeric forms of the amide salt react intramolecularly with the NBr group, for instance, just as the urazole salts do with an alkyl bromide. In this connection it was pointed out by the writer at the Boston meeting of the A. A. A. S., in 1909, that such changes as the Hofmann rearrangement of chloro- and bromoamides, the Lossen rearrangement of hydroxamic derivatives (see L. W. Jones: THIS JOURNAL, **48**, 1, for an excellent dis-

25°. The solutions were varied in concentration from N/3 to N/64. Dr. Chandler found the values $K_i = 0.465$ and $K_m = 0.16$. Dr. Nirdlinger and Dr. Rogers obtained the values $K_i = 0.43$ and $K_m = 0.17$ in their work; the solutions contained small quantities of water, which lowers the reaction velocity. The addition of sodium iodide suppressed the ionization and reaction velocity of the sodium phenylthiourazole practically exactly the amount calculated from our theory; the "salt effect" was "normal" even when three equivalents of sodium iodide were added to one of the sodium urazole (N/64).

We have also made calculations on the excellent data of Tubandt[1] involving the inversion of menthone by sodium ethylate in absolute ethyl alcohol, and have found that both the ethylate ions and the sodium ethylate molecules seem to invert the menthone with the same[2] velocity; that is, $K_i =$

cussion), and also the Beckmann rearrangement of oximes by acids, may be due to a monomolecular rearrangement of the *ion* as well as of the *nonionized salt*.

$$\left\{\begin{matrix} C_6H_5CONKBr \\ \text{and} \\ C_6H_5C(OK) : NBr \end{matrix}\right\} \longrightarrow C_6H_5N : C : O + KBr$$

$$\left\{\begin{matrix} C_6H_5CONBr \\ \text{and} \\ C_6H_5C(O) : NBr \end{matrix}\right\} \longrightarrow C_6H_5N : C : O + Br$$

$$\frac{dx}{dt} = K_i a(C_{salt} - x) + K_m(1 - a)(C_{salt} - x) = [K_i a + K_m(1 - a)](C_{salt} - x)$$

Van Dam (Rec. trav. chim., **18**, 408; **19**, 318) added varying amounts of alkalies to benzbromoamide and found that the reaction velocity increased with an increase in the concentration of the (alkali and) hydroxyl ions. He interpreted the change as a *pure catalysis* by the hydroxyl ions. The writer thinks it much more probable that the benzbromoamide was converted nearly completely into a salt according to the above equations, and that the addition of more alkali simply increased the concentration of the *nonionized salt* in accordance with the Arrhenius isohydric principle, and increased the reaction velocity because the nonionized salt decomposes faster than the ion. The relative magnitudes of K_i and K_m for all such cases should be accurately measured in water and in alcohol. Alcohol will probably be found more satisfactory as a solvent, as in our work, because of the greater changes in the ionization of the salt and the smaller errors involved in K_i and K_m. An article on this subject will soon be published by the writer. (NOTE.—Since this was written, Professor Stieglitz has informed the writer privately that his own experimental work has led him to conclusions similar to ours.)

[1] Ann. Chem. (Liebig), **339**, 41; **364**, 259; **377**, 284. The inversion of menthone by acids seems to involve the ions and molecules of the salt formed by the menthone and the acid.

[2] A similar case seems to be involved in Bredig's study (Z. Elektrochem., **10**, 582) of the change of benzaldehyde into benzoin by cyanides, which he interpreted as being due to a *pure catalysis* by the cyanide ions alone. Although the solvent was 66 per

K_m = 0.41 at 20° and 0.93 at 30°. The solutions containing sodium ethylate in concentrations varying from about 0.05 N to about 0.01 N are dilute enough to be practically ideal solutions, and are probably the ones having the smallest experimental errors; these give excellent data for our theory. The sodium ethylate acts *purely catalytically*, as it is not used up in the reaction. Especially important for the theory is the fact that Tubandt found that added sodium acetate, sodium dimethylhydroresorcinolate, sodium acetoacetic ester and sodium bromide, in various concentrations, have absolutely no "salt effect" on the reaction velocity. This absence of "salt effect" is to be predicted from our theory, and is "normal," whenever the nonionized sodium ethylate and the ethylate ions react with equal velocities; the change produced, by the added salt, in the relative number of ions and molecules of the ethylate can have no effect as long as the ethylate ion and the sodium ethylate molecules are equally active, and their total number remains constant, and no new active constituents are formed. It will be especially important to see whether the ethylate ion from sodium, potassium, lithium and thallium ethylates inverts the menthone with a constant velocity, or constant value for K_i. The values for K_m for the different ethylates may, and probably will, be found to be different, as we have found to be the case with the reactions of alkyl halides with different ethylates and phenolates.

Our theory of alkaline catalysis has been substantiated in still another way by work on imido esters. Stieglitz[1] and Schlesinger found that barium hydroxide decomposes imido esters into nitriles and alcohols, and they used the Ostwald-Arrhenius theory that the decomposition is due to the hydroxyl ions *alone*, as in the case of the saponification of ordinary esters by hydroxides. But we have recalculated their excel-

cent. alcohol, and the concentration of the potassium cyanide varied from 0.05 N to 0.4 N. *Bredig assumed a constant per cent. of ionization of the salt in calculating* K_{cy} or K_i. *This assumption is extremely improbable.* Since there is only a very slight, if any, increase in K_m with increase in V, it is *very probable* that both the nonionized salt and the cyanide ions are active, the value K_i being only slightly, if at all, larger than K_m. It would be extremely interesting to see this problem studied in absolute ethyl alcohol from this point of view, by using a number of cyanides and aldehydes.

[1] THIS JOURNAL, 39, 738.

lent data and have found that the concentration of the barium hydroxide molecules is so small, about 3 to 7 per cent., *that their results can be interpreted fully as well on our theory that both the hydroxyl ions and the nonionized barium hydroxide are, in this case, equally active.* Our theory is completely substantiated in this connection by the work of Dr. E. K. Marshall and Dr. Julia Peachy Harrison, who have found sodium, potassium and lithium ethylates to catalyze the reversible[1] reaction of nitriles with ethyl alcohol,

$$CH_3CN + C_2H_5OH \rightleftarrows CH_3C(:NH)OC_2H_5$$

Just as sodium hydroxide decomposes an imido ester in water into a nitrile and an alcohol, so sodium ethylate, the analogue of sodium hydroxide, decomposes an imido ester in absolute ethyl alcohol *purely catalytically* into a nitrile and an alcohol. The advantage of studying this latter reaction is that the sodium ethylate is far less ionized in ethyl alcohol in the concentrations used than is the sodium hydroxide in aqueous solutions of the same concentrations. This enables us to measure more accurately any possible activity of the sodium ethylate molecules, and when this is done with solutions of sodium ethylate varying from 0.25 N to 0.015625 N we find indeed the values $K_i = 0.344$ and $K_m = 0.228$ for the decomposition of 0.25 N acetimido ethyl ester, and $K_i = 0.1148$ and $K_m = 0.1003$ for the change of 0.25 N benzimido ethyl ester. It should be especially emphasized, in this connection, that the addition of even several molecules of sodium iodide lowers the per cent. of ionization and the reaction velocity, or activity, of the sodium ethylate "normally," or to just the extent calculated from our theory. As was predicted, the "salt effect" of added sodium iodide is very small in this latter case, just as it is in the menthone work (see page 359) and in all cases in which the ethylate ions and the sodium ethylate molecules react with practically equal velocities.

[1] Dr. E. K. Marshall has found this reaction to be reversible in every case studied by him, whether approached from the nitrile or from the imido ester. The equilibrium point varies from 1 per cent. nitrile to 98 per cent. nitrile when different nitriles, and the corresponding imido esters, are used. See Purdie: J. Chem. Soc., **39**, 344. Nef: Ann. Chem. (Liebig,) **287**, 280. Lengfeld and Stieglitz: THIS JOURNAL, **17**, 112. Stieglitz: Ber. d. chem. Ges., **28**, 573. McKee: THIS JOURNAL, **26**, 206; **36**, 209; **42**, 1. Dains: J. Am. Chem. Soc., **31**, 136.

Although this work on the action of ethylates on nitriles and imido esters in ethyl alcohol is presented only tentatively, *as we must work with several other ethylates to be certain that the reaction velocity of the ethylate ion is the same for all ethylates*, these experiments seem to show that both the ethylate ions and the sodium ethylate molecules, and perhaps also both the hydroxyl ions and the barium (sodium, etc.) hydroxide molecules, are concerned in the decomposition of imido esters into nitriles and alcohols.

It may be that both the hydroxyl ions and the nonionized bases react with esters in ordinary saponification.[1] Since the sodium hydroxide, for instance, is very largely ionized in the dilute aqueous solutions used, the activity of the nonionized base may be HIDDEN IN THE EXPERIMENTAL ERRORS on account of its small concentration and small activity. Miss B. Marion Brown is therefore attacking an analogous problem, the saponification of esters and thiol esters with sodium, potassium and lithium sulphydrates in absolute ethyl alcohol, to learn whether *both* the sulphydrate anion and the nonionized metallic sulphydrates react with the esters. The concentration of the nonionized sulphydrate is much larger in concentrated alcoholic solutions than in the corresponding aqueous solutions, and this fact will allow us to measure far more easily the activity of the nonionized sulphydrate towards the esters and secure possibly a deeper insight into the mechanism of the saponification of esters by alkalies.

We are planning the study of the analogous interchange[2] of alkyls when esters are treated with metallic alcoholates in the corresponding absolute alcohol.

$$RCOOCH_3 + NaOC_2H_5 + C_2H_5OH \text{ in excess} \longrightarrow$$
$$RCOOC_2H_5 + NaOCH_3 + C_2H_5OH \text{ in excess} \longrightarrow$$
$$RCOOC_2H_5 + NaOC_2H_5 + CH_3OH$$

[1] Acree and Johnson: THIS JOURNAL, **38**, 344; **39**, 524. This seems clearly to be the case in some recent studies by Holmberg (Z. physik. Chem., **79**, 147) and Johansson (*Ibid.*, **79**, 621) on the removal of halogens from the salts of halogenated acids by the action of alkalies.

[2] Claisen: Ber. d. chem. Ges., **20**, 646. Kremann: Monats. Chem., **26**, 783; **29**, 23. Henriques: Z. angew. Chem., **1898**, 338, 697. Goldschmiedt: Z. Elektrochem., **10**, 221. Kossel, Krüger, and Obermüller: Z. physiol. Chem., **18**, 321; **16**, 153.

The polariscope should be especially useful in studying these changes when the esters are optically active.

These results obtained by the various investigators in the study of the changes of nitriles and of menthone by ethylate are very important for our theory because the sodium ethylate acts as a *pure catalyst* in the older sense in that it is not measurably changed in concentration during the reaction. Notwithstanding this the mechanism of these reactions is essentially the same as that involving the ethylates and the alkyl halides, or the phenolates and the alkyl halides, in which the ethylate and the phenolate are decomposed completely into a sodium halide and an ether. Our theory enables us to predict that there is no essential difference between the cases of old style or pure catalysis, in which the catalyzer is not appreciably used up, and those cases in which the catalyzer is partially or completely changed into the end products.[1] All of the available trustworthy experimental evidence supports this point of view, as the following reasoning will show.

In the reaction of the sodium ethylate or sodium phenolate or sodium thiourazole with the alkyl halides *all of the ethylate or phenolate or urazole salt formed is decomposed with a velocity which is a function of the concentrations of the anions and of the molecules.* In the case of the menthone inversion and the alcohol-nitrile reaction the sodium ethylate does not apparently enter into the reaction and yet its activity is a function of the concentrations of the ethylate anions and of the sodium ethylate molecules. It is very likely, however, that the menthone and the nitrile, or the imido ester in the reverse reaction, actually do react with small amounts of the ethylate ions or sodium ethylate molecules and form salts and ions on account of the unsaturated carbonyl and nitrile groups and the acid character of the imido ester. This is illustrated in the case of the menthone inversion, for instance, by the following brief scheme, in which many possible intermediate reactions are omitted:

[1] For a fuller discussion see Acree and Johnson: THIS JOURNAL, 38, 258; 39, 513. Ber. d. chem. Ges., 41, 3199.

$$\underset{d\text{-menthone}}{C_9H_{18}CO} + \bar{O}C_2H_5 \rightleftarrows \underset{(I)}{C_9H_{18}C(\bar{O})OC_2H_5} \rightleftarrows \underset{l\text{-menthone}}{C_9H_{18}CO} + \bar{O}C_2H_5$$

$$\underset{d\text{-menthone}}{C_9H_{18}CO} + NaOC_2H_5 \rightleftarrows \underset{(M)}{C_9H_{18}C(ONa)OC_2H_5} \rightleftarrows \underset{l\text{-menthone}}{C_9H_{18}CO} + NaOC_2H_5$$

If now only traces of (I) and (M) are formed, the concentrations of (I) and (M) are practically proportional to the products of the concentrations of the menthone and the ethylate ions, and of the menthone and the nonionized sodium ethylate, respectively. The real velocity of the reaction is strictly proportional to the concentrations of the ion (I) and of the nonionized salt (M), and we can repeat the above italicized words and say that *all of the ethylate-menthone compound formed is decomposed with a velocity which is a function of the concentration of the anions* (*I*) *and of the molecules* (*M*). Since we can insert in any equations the product *ethylate ion* × *menthone* instead of (I) and the product *sodium ethylate* × *menthone* instead of (*M*), and since, furthermore, the ethylate ions and sodium ethylate are constantly regenerated and remain in practically constant concentration, it is evident that the reaction velocities in these cases of *pure catalysis* are *apparently* and *indirectly* functions of the concentrations of the ethylate ions and the nonionized sodium ethylate, while *really* and *directly* functions of the concentrations of the ion (I) and the molecule (M), which are decomposed just as the ethylates and the phenolates are decomposed by the alkyl halides. This makes it clear that all cases of catalysis may be treated alike mathematically, the only differences being in the magnitude of the concentrations of (I) and (M), which can range from a small fraction of one per cent. to practically 100 per cent. of the theoretical. The mathematical side of this question has been treated fully in previous articles and is touched briefly again on pages 372–377.

ACID CATALYSIS

The sodium thiourazole and the sodium, potassium and lithium phenolates are formed by the addition of either the

hydroxides or the ethylate of the alkali metal to the corresponding acid; when these salts react with alkyl halides we call these changes *cases of alkaline*[1] *catalysis* in order to compare them with *cases of catalysis by acids*. In the preceding paragraphs it was shown that *in alkaline catalysis we must consider the possibility of reactions of both the anions and the molecules of the reacting salt.*

The writer and Brunel[2] worked on the above ideas of alkaline catalysis and also on the problem that in the catalysis of esters by acids, *we must have traces of intermediate oxonium salts formed, the cations and the molecules of which may be hydrolyzed.* This comparison of acid and alkaline catalysis was published in full in 1907 after further work by Johnson[3] on the decrease of the conductivity of acids by the addition of esters had indicated the formation of these ester salts (I) and (M).

$$CH_3COOR + H + Cl \rightleftharpoons \underset{(I)}{CH_3COOR.H} + Cl \rightleftharpoons \underset{(M)}{CH_3COOR.HCl}$$

It was pointed out that the velocity of saponification is proportional to the concentration of the complex cation, (I), and therefore approximately to the product of the concentrations of the ester and the hydrogen ions, as is observed experimentally in dilute solutions. But the *possibility of the hydrolysis of the nonionized salt, (M), of esters, amides, cane sugar, etc., was also discussed very fully*[4] in several places, and *this idea differentiates our theory from all others ever proposed.* Bredig, Lapworth, Stieglitz, Goldschmidt and Acree had suggested the idea that the complex anions[5] and cations enter into chemical

[1] We mean by *alkaline catalysis* the changes involving hydroxides, ethylates, phenolates, urazole salts, sulphydrates, etc., of the metals and organic bases, whether these be formed in large or small quantities.

[2] Dissertation, Johns Hopkins University, 1905–6. THIS JOURNAL, **43**, 505.

[3] THIS JOURNAL, **38**, 258.

[4] *Ibid.*, **37**, 410; **38**, 265–274, 301, 303, 306, 339, and many other articles.

[5] Kastle was undoubtedly the first to point out that in the saponification of esters and amides, and in the esterification of organic acids, the catalyzing acid forms oxonium or ammonium salts which react with the water or alcohol. He did not take up the question whether these salts undergo changes through their molecules or ions (see P. Am. Assn. Adv. Sci., **47**, 238, for an abstract of the original article, which was never published in full).

reactions, but *we were the first to point out clearly that the nonionized salts may also be concerned in the same reactions*,[1] *and the first to publish the correct application*[2] *of the mass law to all of these cases.*

We pointed out that if (M) were the substance chiefly hydrolyzed the velocity of the reaction would be practically proportional to the product of the concentrations of the cane sugar or ester, hydrogen ions and chloride ions, or, when little organic acid is formed, to the product of the concentrations of the ester and the *square* of the concentration of the hydrogen ions, instead of the *first power* actually observed. We then wrote:[3] "It therefore follows that the undissociated salt, C_m, cannot be the substance which is chiefly undergoing hydrolysis, *although it may do so to a small extent.*" (Italics new!)

With this idea in mind we applied the theory to those cases in which the activity of the nonionized salt increases to such a "large extent" that the reaction velocity is truly practically proportional to the concentration of the nonionized salt, (M), or, for example, to the product of the concentrations of the ester, hydrogen ions and halide ions. The rearrangement of acetylchloroaminobenzene by hydrochloric acid or hydrobromic acid represents such a case:

$$CH_3CONClC_6H_5 + \overset{+}{H} + \overset{-}{Cl} \rightleftharpoons \underset{(M)}{CH_3CONHCl_2C_6H_5} \rightleftharpoons CH_3CONHC_6H_4Cl + \overset{+}{H} + \overset{-}{Cl}$$

and constants were obtained which varied only a few per cent., notwithstanding the fact that the concentrations of the acetylchloroaminobenzene, C_a, hydrogen ions, C_H, and bromide ions, C_{Br}, were each varied nearly 1000 per cent., as the following table[4] shows:

[1] This fact has been emphasized by Stieglitz, for instance, in THIS JOURNAL; **39**, 402–3.

[2] For a discussion of weaknesses in the ideas of Stieglitz, Euler, Zengelis, *et al.*, see THIS JOURNAL, **38**, 342; **39**, 521.

[3] THIS JOURNAL, **38**, 306.

[4] *Ibid.*, **37**, 410; **38**, 265; **41**, 464.

Table V

C_a	C_{Br}	C_H	K
0.00240	0.00234	0.00676	710
0.00400	0.00390	0.00770	700
0.00586	0.00565	0.00900	760
0.00780	0.00746	0.01033	740
0.01134	0.01070	0.01300	720
0.01714	0.01595	0.01760	730
0.02100	0.01940	0.02440	730

Average K = 730

The importance of this case in the study of catalysis was emphasized at that time in these words:[1] "In nearly all catalytic reactions studied heretofore, such as the hydrolysis of esters, inversion of cane sugar, hydrolysis of amides, etc., the velocity of transformation has been found to be simply proportional to the concentration of the hydrogen ions. These two different cases are very important in that they throw light on the theory of catalysis in general and in that they make it possible to determine, in cases where only a small amount of the intermediate compound or salt is present, whether the substance undergoing transformation is the undissociated salt or the ionic form of the salt."

Since that time two researches on acid catalysis have been published by Goldschmidt and by Stieglitz which show very clearly that our theory is a helpful guide for further work. In the esterification of acids and amides the reaction is catalyzed by hydrogen ions, and it has been assumed by Bredig, Lapworth, Goldschmidt, Stieglitz and Acree that the hydrogen[2] ions may combine with the organic acid or amide and form a complex cation, (I), which then unites with the alcohol and forms a complex which yields the ester:

$$CH_3COOH + \overset{+}{H} + \overset{-}{Ac} \rightleftarrows \underset{(I)}{CH_3COOH.\overset{+}{H}} + \overset{-}{Ac} \rightleftarrows \underset{(M)}{CH_3COOH.HAc}$$

$$CH_3CONH_2 + \overset{+}{H} + \overset{-}{Ac} \rightleftarrows \underset{(I)}{CH_3CONH_2^{+}} + \overset{-}{Ac} \rightleftarrows \underset{(M)}{CH_3CONH_2Ac}$$

[1] This Journal, **38**, 267.

[2] For references see Acree and Johnson: This Journal, **38**, 258.

But according to our theory the *nonionized salt* (M) *may also be esterified*, the velocity varying with the substances. In 1909 and 1910 Goldschmidt published some studies on (1) the esterification of formic acid, acetic acid, phenylacetic acid and butyric acid by the catalyzer trichlorobutyric acid, and on (2) the auto-esterification of mono-, di-, and trichloroacetic acids, especially in the presence of the salts of these acids, which, he showed[1] very clearly, proved that the rate of esterification is *practically* proportional to the concentration of (M). If we had known of any one of these cases, Brunel, Johnson and the writer would have interpreted them in 1904–1905 and in 1907 exactly as we do to-day, and exactly as we interpreted *then* the analogous change of acetylchloroaminobenzene, discussed above, and our theory would have had more experimental verification at that time.

A further study of the reactions in (1) and the auto-esterification of formic acid should be of the greatest interest, because there is every indication that both the complex ion (I) and the nonionized complex (M) are esterified side by side with different velocities which can easily be measured,[2] and easily calculated from our equations. The reaction velocities were lowered 65 to 75 per cent. by the addition of the aniline salt: this proves clearly that the per cent. of the reaction velocity due to (I) is much greater than that due to (M). The auto-esterification of mono-, di-, and trichloroacetic acids, with or without added salts, seems to involve practically only (M). Probably in all cases (I) and (M) react side by side. Many examples of reversible and irreversible reactions will be found,

[1] Goldschmidt first considered the esterification of trichloroacetic acids as a catalysis by hydrogen ions (Ber. d. chem. Ges., **29**, 2214), the incorrectness of which was shown by Donnan (Ber. d. chem. Ges., **29**, 2422). Even though it was not till 1909, or two years after our theory appeared in full, that Goldschmidt independently proposed the same explanation "nur als eine Vermutung" (Z. Elektrochem., **15**, 6; Z. physik. Chem., **70**, 627), the writer considers all of Goldschmidt's work on oxidation and reduction, catalysis and the reactions of alkyl halides to involve *more* fundamental conceptions than any other work ever published in physico-organic chemistry.

[2] The disadvantage of this work on esterification is that Goldschmidt cannot measure the *true* concentrations of (I) and (M) and their *real* reaction velocities. We hope to overcome this difficulty in the esterification of the more strongly basic hydrazides and amides, such as $CH_3CON(CH_3)_2$, and this work will have the further advantage that no water is formed as a disturbing factor (THIS JOURNAL, **41**, 468. Reid: *Ibid.*, **41**, 483).

without doubt, in which it can be shown experimentally that only (I) is concerned, and others[1] in which only (M) is appreciably active: and still many others will be found in which *both* the cation (I) and the molecule (M) can easily be shown to be active, as we have reported above to be the case in some of our cases of alkaline catalysis.

Just as we have proven experimentally for our cases of alkaline catalysis, it is very important that our theory holds *both* for (*a*) *pure catalysis* by acids in Goldschmidt's studies of esterification and in saponification, in which only *traces* of the intermediate compounds (I) and (M) are formed, and also for (*b*) the examples in which the amount of salt formed by the acid is very large and can be accurately measured, as in Stieglitz's work, which will now be discussed.

A very important line of evidence for our theory of acid

[1] In 1907 we interpreted (THIS JOURNAL, **29**, 523, lines 20–21) the change of diazoaminobenzene into aminoazobenzene by aniline hydrochloride in aniline (Goldschmidt: Ber. d. chem. Ges., **21**, 1016, 2557; **25**, 1347; **29**, 1369, 1899. Z. physik. Chem., **29**, 89; **70**, 627. Ann. Chem. (Liebig), **351**, 108) as a reaction of a nonionized salt analogous to the rearrangement of acetylchloroaminobenzene by hydrochloric acid described above. Goldschmidt had previously interpreted it as a catalysis by hydrogen ions (Ber. d. chem. Ges., **29**, 1905), and later showed that perhaps the nonionized acid must be considered (Z. physik. Chem., **29**, 118). Finally, in 1910, he too came to the conclusion that it is a reaction of a *nonionized salt*, which he supposed to be the nonionized aniline salt (Z. physik. Chem., **70**, 643). Because of the equilibrium equation,

$$C_6H_5NH_2.HCl \times C_6H_5N : NNHC_6H_5 = C_6H_5N : NNH_2ClC_6H_5 \times C_6H_5NH_2 \times K$$

we reasoned that the substance transformed slowly is not necessarily the nonionized aniline hydrochloride, but perhaps the nonionized hydrochloride of the diazoaminobenzene, this kind of reaction being found quite frequently in pentavalent nitrogen derivatives. The $C_6H_5N : N-$ group, just like the other negative groups, migrates into the benzene ring in the para position:

$$(C_6H_5N : N).NHC_6H_5 \longrightarrow HNHC_6H_4.N : NC_6H_5$$
$$\quad\quad H\ Cl \quad\quad\quad\quad H\ Cl$$
$$(NO_2)NHC_6H_5 \longrightarrow HNC_6H_4NO_2$$
$$\quad H\ Cl \quad\quad\quad H\ Cl$$
$$(Cl)N(COCH_3)C_6H_5 \longrightarrow HN(COCH_3)C_6H_4Cl$$
$$\quad H\ Cl \quad\quad\quad\quad H\ Cl$$

The exact mechanism of all these migrations has not yet been learned, and the writer has a number of views which will be tested quantitatively. It does not seem absolutely certain, for instance, that Goldschmidt has sufficient evidence to disprove the idea that in the rearrangement of the diazoaminobenzene by aniline hydrochloride there may be a trace of the diazonium chloride present as an equilibrium constituent which reacts *reversibly* and rapidly with the amino group of the aniline, but *irreversibly* and slowly with the benzene nucleus.

catalysis is all of the fine experimental work of Stieglitz,[1] and of his collaborators, on the catalysis of imido ester salts, to which chemists should give the highest consideration. It will be recalled that Stieglitz found that the reaction is not purely that of the cation, and that he attempted to explain this deviation, or so-called "salt catalysis," by using the Arrhenius-Euler[2] hypothesis that the water reacts only through its hydrogen and hydroxyl ions,

$$C_6H_5C(:\overset{+}{N}H_2)OCH_3 + \overset{+}{H} + \overset{-}{O}H \longrightarrow C_6H_5COOCH_3 + \overset{+}{N}H_4$$

and that the cations of the salts increase the per cent. of ionization, or K_w, and hence active mass, of the water and in this way increase the velocity of the saponification. It has been pointed out by the writer[3] that this explanation probably involves a fundamental error: the error is the assumption that the water must react through its ions alone, and can change in ionization as much as is demanded by Stieglitz's explanation of his results. (1) Such an assumption, in connection with well known cases of reactions involving water directly or indirectly, leads to the contradictory conclusion that *the same cation in the same concentration must in one case* INCREASE *and in another case* DECREASE *the value of* K_w. (2) Lorenz and Böhi[4] made direct measurements of the ionization of water in the presence of various amounts of salts, acids and bases by the use of the hydrogen electrode and found values for the ionic concentration of water at 0°, 18° and 25° which agreed within 6 per cent., or within the experimental errors, with those obtained by Kohlrausch in his measurement of the conductivity of pure water. (3) Stieglitz's own experimental work gives the best evidence against the theory that the water reacts only through its ions, which are increased in concentration by added salts. The hydrochloride of ethyl iminobenzoate is a typical case and gives the constants[5] 15.4×10^{-5},

[1] THIS JOURNAL, **39**, 29, 166, 402, 437, 586, 719. J. Am. Chem. Soc., **32**, 221.

[2] Euler: Z. physik. Chem., **32**, 348. Arrhenius: *Ibid.*, **1**, 110; **4**, 226; **31**, 197.

[3] See THIS JOURNAL, **41**, 475, for a general discussion of this question, which will be amplified in our detailed report.

[4] Z. physik. Chem., **60**, 733.

[5] Derby: THIS JOURNAL, **39**, 470–1.

136×10^{-5}, and 307×10^{-5} at 0°, 18° and 35°, respectively. When these figures are substituted in the equation[1] $K_T = K_{T_0} \times 10^{(T-T_0)C}$ we find the values $C = 0.0525$ and $C = 0.0520$, for the intervals 0°–18° and 0°–25°, respectively. These are perfectly normal values for C, about like our value $C = 0.0526$ for the reaction of methyl iodide and sodium phenolate, for instance. Since, however, K_w for water at 0°, 18° and 25° is about 0.12×10^{-14}, 0.64×10^{-14} and 1.2×10^{-14}, respectively, the reaction velocities 136 and 307 must be divided by 5.3 and 9.6 to make equal and comparable the factor for the ionized mass of the water at 0°, 18° and 25°. When this is done, we find for the intervals 0°–18° and 0°–25° the values $C = 0.0120$ and $C = 0.0127$, respectively, which *are* LESS THAN ONE-FOURTH THE NORMAL VALUE *0.0526 found in our reactions, for instance.* To state it another way, if the reaction velocities of imido ester salts actually have normal temperature coefficients and his interpretation is correct, then Stieglitz should have found values at 18° and 25° which, compared with those found at 0°, were 5.3 and 9.6 times as large as those actually observed. In the light of these three lines of evidence the interpretation given by Stieglitz to these phenomena appears to the writer to be plainly untenable.

Now all the *published* work of Stieglitz and his coworkers fits our theory very nicely, and gives excellent evidence, without any faulty assumptions, that both the imido ester cations and the nonionized imido ester salts are saponified in the following way:

$$C_6H_5C(:\overset{+}{N}H_2)OC_2H_5 + H_2O \longrightarrow C_6H_5COOC_2H_5 + \overset{+}{N}H_4$$

$$C_6H_5C(:NH_2Cl)OC_2H_5 + H_2O \longrightarrow C_6H_5COOC_2H_5 + NH_4Cl.$$

By using Stieglitz's latest values,[2] Dr. C. N. Myers has found for the benzimidonium ethyl ester chloride, bromide and nitrate the figures $K_i = 162$ and $K_m = 50.3$, $K_i = 163.8$ and K_m 46.5, $K_i = 163.2$ and $K_m = 48.2$, respectively. These values of K^i are identical within the experimental errors; they should be identical because all three salts yield the same cation.

[1] Hecht and Conrad: Z. physik. Chem., **3**, 465.
[2] J. Am. Chem. Soc., **32**, 224.

Not only does our theory interpret his experimental results properly when the imido ester salt alone is hydrolyzed, but also, as far as we can calculate from his published results, when added hydrochloric acid, potassium chloride, potassium bromide, lithium chloride, etc., increase the "salt effect." Stieglitz wrote:[1] "We arrived thus *empirically at the rather unexpected result* (italics ours) that the accelerating factor A is approximately the same for the sodium, potassium and lithium chlorides and for the bromides as well as for the chlorides, viz., about 185 per cent. per gram molecule of fully ionized salt." But these facts, instead of being "empirical" and "rather unexpected" to us, were *predicted* from our theory, since the per cent. of ionization and hence reaction velocity of the imido ester salt would be the same in all of these cases. Our theory gives, then, a perfecty rational explanation of their so-called "salt effect" and proves it to be "normal"[2] and due *chiefly*, as in our work, *to the reaction of the nonionized imido ester salt, which Stieglitz did not take into consideration in his theory.*[3] Dr. C. N. Myers and the writer will soon publish in a separate article all of the mathematical details of this new interpretation of the reactions of imido esters.

Since the reactions of Stieglitz and his coworkers have nearly normal temperature coefficients it is evident that their work proves the water to react *chiefly* through its molecules,[4]

[1] J. Am. Chem. Soc., **32**, 223.

[2] At the New York meeting of the Int. Cong. Appl. Chem. Professor Stieglitz reported that his unpublished and most accurate data on the effect of added salts show that there is a deviation, or, as we say, an "abnormal salt effect," analogous to that found in some of our reactions.

[3] We called attention four years ago to the possibility of the reaction of the nonionized imidoester salt (THIS JOURNAL, **39**, 521).

[4] When the mass law holds for the reactions

$$C_6H_5C(:\overset{+}{N}H_2)OCH_3 + H_2O \rightleftharpoons C_6H_5C(:NH)OCH_3 + H_2O.\overset{+}{H}$$

$$C_6H_5C(:NH_2Cl)OCH_3 + H_2O \rightleftharpoons C_6H_5C(:NH)OCH_3 + H_2O.HCl$$

it is impossible to tell from the data whether the products on the left of the arrows or the ones on the right, or both, yield the end products (Acree: THIS JOURNAL, **39**, 302. Goldschmidt and Sunde: Ber. d. chem. Ges., **39**, 711. Goldschmidt and Udby: Z. physik. Chem., **60**, 728). We shall consider only the compounds on the left in our interpretation because nothing is known about the ionization of $H_2O.HCl$, and because Stieglitz's values for the ionization and reaction velocities of the imido ester salts harmonize with our theory.

as discussed in the preceding section (3). We may assume the ions of the water to enter into these changes to a certain extent, which may be determined by the *difference* between the *observed* temperature coefficient and the *real* temperature coefficient of the reaction between *given concentrations* of the imido ester cation, nonionized salt, hydrogen ions and hydroxyl ions. This same reasoning could be applied to a large number of cases of reactions of water and analogous substances, in order to learn to what extent the ions and the molecules of the substance are concerned in the changes, provided the necessary experimental data can be secured.

PHYSICAL CATALYSIS

The question how the particles come together before reaction takes place is very important. We have for several years believed with Michael and others that the alkyl halide may actually combine with the phenolate anion, for example, (or sodium phenolate molecule), and form at least a trace of a highly reactive complex ion (or molecule). Expressed in the ideas of J. J. Thomson, it may be that the alkyl halide and phenolate anion must come close enough together to allow an interchange or disturbance of electrons.[1] In the same way a mechanical disturbance, or a disturbance of the electrons through "electrostatic induction" by the electrolytes[2] present,

[1] For central ideas in this connection see: J. J. Thomson: "The Corpuscular Theory of Matter", pp. 120–141 (1907). Science, **30**, 257. Fry: Z. physik. Chem., **78**, 385–397; 398–412. J. Am. Chem. Soc., Proceed., **30**, 34. *Ibid.*, **34**, 664. Falk and Nelson: J. Am. Chem. Soc., **33**, 1637–1654; **33**, 1140. School of Mines Quarterly, **30**, 179–198. For some interesting applications see L. W. Jones: THIS JOURNAL, **48**, 25–27. For a very suggestive discussion see L. G. Winston. THIS JOURNAL, **45**, 547. For a comprehensive report see W. W. Strong: THIS JOURNAL, **44**, 85. See Nef: J. Am. Chem. Soc., **28**, 1549; **30**, 645, for very important ideas connecting his theory of bivalent carbon with a practical equivalent of the electron theory. Julius Meyer: Z. physik. Chem., **60**, 81; **67**, 257. Kraus: J. Am. Chem. Soc., **29**, 1557; **30**, 653, 1197, 1323.

[2] J. J. Thomson: "The Corpuscular Theory of Matter", p. 135. L. G. Winston: THIS JOURNAL, **45**, 547. This idea of a *physical catalysis* by electrolytes was proposed by the writer in 1908 and 1909 (THIS JOURNAL, **39**, 308–9). "..... *a catalyzer may influence the velocity of a reaction physically*..... by imparting energy to, or removing it from, the system." (*Ibid.*, **41**, 483): "Finally, one other salt effect must be considered. The thermodynamic potential, or 'activity,' or driving force behind each reaction depends not only upon the substances themselves but upon the surrounding *field*. When this is changed by the addition of electrolytes or nonelectrolytes there will be a change in the corresponding thermodynamic potential and therefore in the reaction velocity, although this will in many cases be negligible." It may be negligible in the dilute solutions and become more and more noticeable, if at all, as the concentration increases.

might so change the arrangement of the atoms and electrons of a molecule of alkyl halide and of another sodium phenolate that a point of one molecule would, *in effect*, become momentarily negative and a point of the other positive:[1] hence the two could combine electrically and react further. Perhaps the molecules can combine without any such electronic disturbance or transfer; J. J. Thomson says[2] that "We thus see that it is possible to have forces electrical in their origin binding the two systems together without a resultant charge on either system," and this idea may be extended to molecules. Substantial evidence for such an idea was found in the isolation and study of Scholl[3] and Steinkopf's double compound of silver nitrate and cyanomethyl iodide, which was found to change readily in the solid state or in solution into cyanomethyl nitrate and silver iodide.

In developing the equations which we should use we may consider the case first in which the alkyl halide reacts with the phenolate anion. If these unite to form a complex anion in very small traces and we represent the concentrations by the formulas, the equation

$$(a)\quad CH_3I \times An = K \times CH_3I.An$$

holds approximately for any given concentration even though the value of the "stability constant" K is not constant for all concentrations. We cannot measure K experimentally at present and our only reason for thinking that K should remain constant for nearly all concentrations is that the applica-

[1] This idea was proposed in 1908 (address at the Baltimore meeting of the A. A. A. S., December, 1908. Science, **30**, 624) to explain, for instance, the addition of chlorine or hydrogen to ethylene,

$$CH_3 : CH_2 + Cl_2 \longrightarrow \overset{+}{C}H_3.\overset{+}{C}H_2 + 2\overset{-}{C}l \longrightarrow C_2H_4Cl_2$$

We suggested at that time the use of electromotive force methods to study this and similar problems, and since then Dr. L. J. Desha, Dr. N. E. Loomis, and Dr. C. N. Myers have made a number of measurements of the sytems $Pt—H_2—HCl—C_2H_4—Pt$, $Pt—Cl_2—HCl—C_2H_4—Pt$, and $Pt—O_2—NaOH—C_2H_4—Pt$. In all of these cases we have secured rather constant values, which range from 0.55 volt to 0.85 volt. We shall not feel justified in publishing the data until we can prepare *very pure ethylene* and prove beyond question that the electromotive force truly represents the above reactions, and does not arise from small traces of oxygen and other impurities in the ethylene.

[2] "The Corpuscular Theory of Matter", pp. 121, 127, 130 and 135.

[3] Ber. d. chem. Ges., **39**, 4393. Hantzsch and Caldwell: *Ibid.*, **39**, 2472. Acree and Loy : THIS JOURNAL, **45**, 224.

tion of the mass law has shown that the stability constants of most complex salts, such as double cyanides, complex ammonium salts, etc., are fairly constant. If this complex yields the end products the following equations hold approximately, whether the complex salt is formed slowly (either reversibly or irreversibly) and decomposes rapidly, or is formed rapidly reversibly and decomposes slowly:

$$(b)\quad \frac{dx}{dt} = K'_i \times CH_3I.An$$
$$= K'_i/K \times CH_3I \times An$$
$$= K_i \times CH_3I \times An$$

But this is exactly the equation that we get if the alkyl halide and anion react directly without the formation of an intermediate complex anion. In the one case our reaction velocity constant $\frac{K_i}{K}$ is the quotient of two constants, both of which (or the quotient) are assumed to be constant for all concentrations: in the other case we make no *assumptions* other than the constancy of the reaction velocity K_i, the validity of which assumption is tested experimentally.

In the present studies, however, the above equation fails to represent the entire reaction, and we may therefore consider the possibility of the reactions of nonionized substances. It might well be that the *nonionized* double salt,

$$CH_3I.NaOC_6H_5,$$

can decompose *in solution* into sodium iodide and phenyl methyl ether just as we have shown the *solid* (and presumably *nonionized*) cyanomethyl iodide-silver nitrate double compound to yield silver iodide and cyanomethyl nitrate. We may consider this nonionized double salt to be formed by the union of the alkyl halide with the sodium ions and phenolate ions, or by the union of the alkyl halide with the nonionized sodium phenolate. These two processes are represented as follows:

$$(c)\quad CH_3I \times \overline{O}C_6H_5 \times \overset{+}{N}a = K' \times CH_3I.NaOC_6H_5, \text{ and}$$
$$(d)\quad CH_3I \times NaOC_6H_5 = K'' \times CH_3I.NaOC_6H_5$$

It is clear that if sodium phenolate obeyed Ostwald's dilution law, and the equation

$$\overset{+}{Na} \times \overset{-}{O}C_6H_5 = K'' \times NaOC_6H_5 = \frac{K'}{K''} \times NaOC_6H_5$$

were true for all concentrations, K' and K'' also being constant, we could not possibly tell which of these two processes is taking place. The reaction (*c*) would be written

$$(e) \quad \frac{dx}{dt} = K'_m \times CH_3I.NaOC_6H_5$$

$$= \frac{K'_m}{K'} \times CH_3I \times \overset{-}{O}C_6H_5 \times \overset{+}{Na}$$

$$= \frac{K'_m K''}{K'} \times CH_3I \times NaOC_6H_5$$

$$= \frac{K'_m}{K''} \times CH_3I \times NaOC_6H_5 = K_m \times CH_3I \times NaOC_6H_5$$

The reaction (*d*) would be written:

$$(f) \quad \frac{dx}{dt} = K'_m \times CH_3I.NaOC_6H_5$$

$$= \frac{K'_m}{K''} \times CH_3I \times NaOC_6H_5 = K_m \times CH_3I \times NaOC_6H_5$$

which would also hold true even if no complex salt were formed as an intermediate product. If the sodium phenolate obeyed the Ostwald dilution law these two equations could be used interchangeably and we could not know whether the sodium phenolate reacts through the sodium and phenolate ions together, or through its nonionized portion, or through both processes together, and we could not know whether a trace of the complex salt is an intermediate product. Sodium phenolate does not obey the Ostwald dilution law and these equations (*e*) and (*f*) are not identical by any means. If equations (*b*) and (*c*) represent the true reactions the total reaction can be represented by the equation (*g*) if α is the ionization, and $(A—x)$ is the concentration of the sodium phenolate, and $(B—x)$ is the concentration of the alkyl halide, at the time t, and x is zero when t is zero.

$$(g)\quad \frac{dx}{dt} = K_i\alpha(A-x)(B-x) + K_m\frac{\alpha^2}{V}(A-x)(B-x)$$

$$= \left[K_i\,\alpha + K_m\frac{\alpha^2}{V}\right](A-x)(B-x), \text{ or}$$

$$K_V = K_i\,\alpha + K_m\frac{\alpha^2}{V} = \frac{B}{t(A-B)}\log_n\frac{B(A-x)}{A(B-x)}$$

Equation (*h*) holds true if equations (*b*) and (*f*) represent the two side reactions:

$$(h)\quad \frac{dx}{dt} = K_i\alpha(A-x)(B-x) + K_m(1-\alpha)(A-x)(B-x)$$

$$= [K_i\alpha + K_m(1-\alpha)](A-x)(B-x), \text{ or}$$

$$K_V = [K_i\alpha + K_m(1-\alpha)] = \frac{B}{t(A-B)}\log_n\frac{B(A-x)}{A(B-x)}$$

If we inspect equations (g) and (*h*) carefully we see that they become more and more nearly identical as the salt comes closer and closer to obeying the Ostwald dilution law, as pointed out above. When they become nearly, or quite, identical the values of K_V, K_i and K_m in both equations (g) and (*h*) become nearly or quite *constant*, within the experimental errors, and hence it is impossible to decide, from the equations alone, which of the two interpretations of the reaction is correct. If we inspect equation (g) closely we see that it has the same form as the one demanded by the Arrhenius-Euler theory of salt catalysis which Stieglitz has used so successfully in his fine work on the imido esters, and this fact accounts for his success in obtaining any constants at all in his work. *When equation (g) is applied to our work we secure constants in only two cases,*[1] *but equation (h) gives satisfactory constants in every case studied by us up to this time, and also in all of Tubandt's, Goldschmidt's, and Stieglitz's published work. For that reason we believe that we have secured valid evidence for the theory that we must consider the possibility of the reactions of both ions and molecules in all reactions.* Whether in the two particular cases mentioned the alkyl halide does actually react with both ions together, perhaps along with the nonionized molecules, or

[1] Even certain corrections for fluidity have not aided us.

whether it is a case of an "arithmetical accident" cannot be said at present.

We are presenting our results merely in the light of what has been accomplished. We are studying the effect of physical factors such as viscosity and fluidity, and are extending the investigations to solutions more dilute than N/64 and hope that we shall be able to investigate some of them as dilute as N/1024. If the theory is found to hold over the entire range from N/1 to N/1024, even in the presence of added salts, we shall then feel that we have a working hypothesis by which to study all reactions. In some other cases, as pointed out before,[1] it may be found that the main reaction is disturbed, or that a so-called "abnormal salt catalysis" is produced, on account of an electronic disturbance, or of the formation of still other complex compounds, in *traces* in some cases, the ions or molecules of which have reaction velocities greater or smaller than those of the original constituents. The formulas

$$CH_3I.C_2H_5ONa.NaI, \quad CH_3I.C_2H_5ONa.\overset{+}{N}a \text{ and}$$
$$C_6H_5C(:NH_2Cl)(OC_2H_5).KCl$$

are illustrations, and the variations of this central idea are manifold.

In Table VI are given the values of K_i and K_m found in the work in this laboratory, while in Table VII are given the values of K_i and K_m which we have calculated from the work of other investigators:

[1] For references see Acree: This Journal, 41, 475.

Table VI

Reaction	Observer	K_i	K_m
(1) Sodium ethylate and methyl iodide at 25°	Dr. H. C. Robertson	0.127 [1]	0.0594
(2) The same	Miss B. Marion Brown	0.1294	0.0573
(3) Potassium ethylate and methyl iodide at 25°	Dr. Julia P. Harrison	0.127	0.066
(4) Sodium ethylate and ethyl iodide at 25°	Dr. E. K. Marshall	0.0120	0.00427
(5) The same	Mr. J. H. Shrader	0.0122	0.00404
(6) Sodium ethylate and ethyl bromide at 25°	Dr. E. K. Marshall	0.00576	0.00233
(7) Sodium phenolate and methyl iodide at 25°	Dr. H. C. Robertson	0.0282	0.00474
(8) Potassium phenolate and methyl iodide at 25°	Dr. H. C. Robertson and Mr. J. H. Shrader	0.0283	0.0037
(9) Lithium phenolate and methyl iodide at 25°	Dr. H. C. Robertson and Mr. J. H. Shrader	0.0284	0.0040
(10) Sodium phenolate and methyl iodide at 25°	Dr. H. C. Robertson	0.091	0.0131
(11) Sodium phenolate and ethyl iodide at 25°	Dr. H. C. Robertson	0.0056	0.00099
(12) The same at 35°	Dr. H. C. Robertson	0.0184	0.00323
(13) Sodium phenylthiourazole and ethyl iodide at 25°	Dr. J. Chandler	0.465	0.16
(14) The same (in aqueous alcohol) at 25°	Dr. Sidney Nirdlinger and Dr. F. M. Rogers	0.43	0.17
(15) Sodium ethylate and acetimido ethyl ester at 25°	Dr. E. K. Marshall	0.344	0.228
(16) Sodium ethylate and benzimido ethyl ester at 25°	Dr. Julia P. Harrison	0.1148	0.1003
(17) Acetylchloroaminobenzene and hydrobromic acid at 3°	Dr. J. M. Johnson	Very small	730

[1] The values in brackets should be, and are, practically identical. K_i and K_m involve in some cases a small "abnormal salt effect" which will be discussed in the final report.

Table VII

Reaction	Observer	K_i	K_m
(18) Inversion of menthone by sodium ethylate	C. Tubandt	0.41 at 20° 0.93 at 30°	0.41 at 20° 0.93 at 30°
(19) Rearrangement of diazoaminobenzene into aminoazobenzene by aniline hydrochloride in aniline at 25°, and many other similar examples	H. Goldschmidt	Very small	0.06
(20) Auto-esterification of trichloroacetic acid in absolute ethyl alcohol at 25°	H. Goldschmidt	Very small	0.026
(21) Esterification of acetic acid by trichlorobutyric acid in the presence of its aniline salt in absolute ethyl alcohol at 25°	H. Goldschmidt	Ionic reaction suppressed by aniline salt	About 0.0073 for 1.0 N trichlorobutyric acid
(22) Esterification of phenylacetic acid by trichlorobutyric acid in the presence of its aniline salt in absolute ethyl alcohol at 25°	H. Goldschmidt	Ionic reaction suppressed by aniline salt	About 0.00055 for 1.0 N trichlorobutyric acid
(23) Esterification of *n*-butyric acid by trichlorobutyric acid in the presence of its aniline salt in absolute ethyl alcohol at 25°	H. Goldschmidt	Ionic reaction suppressed by aniline salt	About 0.0038 for 1.0 N trichlorobutyric acid

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Table VII—(Continued)

Reaction	Observer	K_t	K_m
(24) Esterification of formic acid by trichlorobutyric acid in the presence of its aniline salt in absolute ethyl alcohol at 25°	H. Goldschmidt	Ionic reaction suppressed by aniline salt	About 0.125 for 1.0 N trichlorobutyric acid
(25) Saponification of benzimidonium ethyl ester chloride at 25°	J. Stieglitz	[162.0] [1]	50.3
(26) Saponification of benzimidonium ethyl ester bromide at 25°	J. Stieglitz	163.8	46.5
(27) Saponification of benzimidonium ethyl ester nitrate at 25°	J. Stieglitz	[163.2]	48.2
(28) A number of other reactions described by Stieglitz and his coworkers, at other temperatures, and in the presence of various salts, hydrochloric acid, etc.	J. Stieglitz and coworkers	.....	.....
(29) Change of benzaldehyde into benzoin by potassium cyanide	Bredig and Stern	About 0.089	About 0.089

[1] The values in brackets should be, and are, practically identical. The values are given in terms of Stieglitz's constants.

Acree

OBITUARY

PAUL ÉMIL LECOQ DE BOISBAUDRAN[1]

Paul Émil Lecoq de Boisbaudran, the discoverer of the element gallium, died in Paris on May 28, 1912. He was born at Cognac, Charente, on April 18, 1838, and was therefore 74 years old at the time of his death. His early education was entirely neglected and at the age of 15 he entered the employ of his father, who conducted a liquor store. He devoted all his spare time to scientific studies, however, and finally secured a place in the laboratories of the University of Paris. Here he remained three months, casting longing eyes on the collection of rare earths gathered there but to which he was denied access on account of his inexperience and deficient preparation. He then went to Würtz in the École de Médecine, and it was here, in 1875, that he discovered gallium in a Pierrefitte blende.

He never occupied any official position and all his work was done without help from assistants or students. The results of his investigations were published in numerous short isolated articles and many have therefore not secured the attention and recognition which they deserve.

In 1876 he was awarded the Cross of the Legion of Honor for his discovery of gallium. In 1872 the Paris Academy of Sciences voted him the Bordin Prize and in 1880 the La Caze Prize. Two years earlier he had been elected Corresponding Member. In 1879 he was given the Davy Medal.

The last years of his life were spent in La Combe and in Paris where, in a small private laboratory, he devoted all his leisure time to his investigations.

While his scientific activities were many-sided, including such subjects as gravity, meteorology and problems in agricultural chemistry, he was preëminently a physical chemist and he stands by the side of Kirchhoff, Bunsen and Sir W. Crookes as one of the founders of Spectrochemistry. In this connection may be mentioned the relations, first pointed out by him, between the spectra of elements and their atomic weights, and the development of the method for the investigation of the spark spectra of solutions. This method led to his discovery of gallium, a discovery which fitted in so brilliantly with Mendeléef's system, although Lecoq de Boisbaudran's work was in no wise suggested by this theory. Attention should

[1] This note is based on an admirable sketch by Prof. G. Urbain in the Chem. Ztg., 36, 929–933.

also be called to his investigations on cathodic phosphorescence phenomena which involved the idea of solid solutions, now generally considered quite a modern conception; on the applications of electrolysis to chemical analysis; and on supersaturation. The work to which he devoted the greater part of his life and which is best known is, of course, that on the rare earths, in the course of which he discovered two other new elements, samarium and dysprosium.

REVIEWS

MESSUNGEN ELEKTROMOTORISCHER KRÄFTE GALVANISCHER KETTEN MIT WÄSSERIGEN ELEKTROLYTEN. Gesammelt und bearbeitet im Auftrage der Deutschen Bunsen-Gesellschaft von R. ABEGG, FR. AUERBACH, R. LUTHER. Halle a. S.: Verlag von Wilhelm Knapp. 1911. Price, M. 8.40.

No man interested in electrochemistry can afford to be without this book. The first part deals with the literature on electromotive-force measurements in aqueous solutions and contains nearly all references of any value. The second part deals with the experimental data obtained by various workers, and the third part gives the electrode potentials arranged according to elements and also according to increasing values. The names of the authors are a guarantee of the importance of this volume. S. F. ACREE

OUTLINES OF ORGANIC CHEMISTRY. A Book Designed Especially for the General Student. By F. J. MOORE, PH.D., Associate Professor of Organic Chemistry in the Massachusetts Institute of Technology. New York: John Wiley & Sons; London: Chapman & Hall, Limited. 1910. pp. v + 315. Price, $1.50.

This book was designed to meet the needs of students specializing in Physics, Biology and Sanitary Engineering. For that reason the author has omitted several important subjects, such as the acetoacetic ester synthesis, the Grignard reaction, and *cis-trans* isomerism. All of the classes of compounds taken up, however, are of the greatest economic and scientific value, and the treatment of these subjects is clear and interesting. The reviewer finds especially praiseworthy the constant use of the graphical formula, the chapter on amino acids and proteins, and that on the organic chemistry of vital processes. S. F. ACREE

ERRATUM

Plates VIII and X, facing pp. 117 and 119, should be interchanged.